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#23	Search **(her-2/neu and hyrbid)** Limits: **Publication Date to 1999/1/29**	08:41:16	439
#7	Search **(her-2/neu and chimera)** Limits: **Publication Date to 1999/1/29**	08:41:05	1
#22	Search **(p185 and chimera)** Limits: **Publication Date to 1999/1/29**	08:39:46	1
#21	Search **(p185 and hybrid)** Limits: **Publication Date to 1999/1/29**	08:39:38	0
#20	Search **(erb B2 and hybrid)** Limits: **Publication Date to 1999/1/29**	08:38:59	1
#19	Search **(erb B2 and chimera)** Limits: **Publication Date to 1999/1/29**	08:38:51	0
#18	Search **(erb B2 and chimera or hybrid)** Limits: **Publication Date to 1999/1/29**	08:38:45	41440
#15	Search **(erb B2 and fusion)** Limits: **Publication Date to 1999/1/29**	08:37:27	2
#14	Search **(p185 and fusion)** Limits: **Publication Date to 1999/1/29**	08:35:43	20
#8	Search **(her-2/neu and fusion)** Limits: **Publication Date to 1999/1/29**	08:32:13	5
#6	Search **(her-2/neu and chimeric or fusion protein)** Limits: **Publication Date to 1999/1/29**	08:31:05	49776
#4	Search **(p185 or (erb B2) or her-2/neu and chimeric protein)** Limits: **Publication Date to 1999/1/29**	08:28:35	398
#3	Search **(p185 or (erb B2) or her-2/neu and fusion protein)** Limits: **Publication Date to 1999/1/29**	08:28:26	401
#2	Search **(p185 or (erb B2) or her-2/neu and fusion)** Limits: **Publication Date to 1999/1/29**	08:28:10	401
#1	Search **p185 or (erb B2) or her-2/neu and fusion** Limits: **Publication Date to 1999/1/29**	08:27:55	401

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☐	L14	(L13 and neu)	1728
☐	L13	((her adj 2) and fusion)	2402
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☐	L12	L11 and her-2	2
☐	L11	L10 and fusion	7
☐	L10	5976546	9
	DB=EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ		
☐	L9	WO 9602555	2
☐	L8	WO 9517210	3
☐	L7	WO 9118926	3
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	DB=USPT; PLUR=YES; OP=ADJ		
☐	L5	(L4 and hybrid)	0
☐	L4	(L3 and chimera)	2
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       03aug06 15:53:17 User290558 Session D65.1
            $0.34    0.097 DialUnits File1
     $0.34  Estimated cost File1
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     $0.53  Estimated cost this search
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         (c) format only 2006 Dialog
  File 159:Cancerlit 1975-2002/Oct
         (c) format only 2002 Dialog
 *File 159: Cancerlit is no longer updating.
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S ((ERB (N) B2) OR (HER (N) 2) AND CHIMERA OR FUSION)
Processing
Processed  10 of  10 files ...
Completed processing all files
           9657  ERB
          72649  B2
           1661  ERB(N)B2
         240964  HER
       15300474  2
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          14803  HER(N)2
          46428  CHIMERA
         517373  FUSION
      S1 519033  ((ERB (N) B2) OR (HER (N) 2) AND CHIMERA OR FUSION)
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S (ERB (N) B2) OR (HER (N) 2)
Processing
Processed  10 of  10 files ...
Completed processing all files
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          72649  B2
           1661  ERB(N)B2
         240964  HER
       15300474  2
          14803  HER(N)2
      S2  16318  (ERB (N) B2) OR (HER (N) 2)
?

S S2 AND (FUSION (N) PROTEIN)
Processing
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         517373  FUSION
        6824809  PROTEIN
          94590  FUSION(N)PROTEIN
      S3    107  S2 AND (FUSION (N) PROTEIN)
?

RD S3
      S4     57  RD S3  (unique items)
?

S (IMMUNE (N) RESPONSE) AND S4
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         4806444  RESPONSE
          358922  IMMUNE(N)RESPONSE
              57  S4
      S5       6  (IMMUNE (N) RESPONSE) AND S4
?

RD S5
      S6       6  RD S5  (unique items)
?

TYPE S6/FULL/1-6

  6/9/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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15525515   PMID: 15994974
 A single vaccination with polyomavirus VP1/VP2Her2 virus-like particles
 prevents outgrowth of HER-2/neu-expressing tumors.
  Tegerstedt Karin; Lindencrona Jan Alvar; Curcio Claudia; Andreasson Kalle
; Tullus Carl; Forni Guido; Dalianis Tina; Kiessling Rolf; Ramqvist
Torbjorn
  Department of Oncology-Pathology, Karolinska Institutet, Cancer Centrum
Karolinska, Stockholm, Sweden.
  Cancer research (United States) Jul 1 2005, 65 (13) p5953-7, ISSN
0008-5472--Print  Journal Code: 2984705R
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Contract/Grant No.: R01CA102280; CA; NCI
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

Murine polyomavirus (MPyV) VP1 virus-like particles (VLPs), containing a fusion protein between MPyV VP2 and the extracellular and transmembrane domain of HER-2/neu (Her2), Her2(1-683)PyVLPs, were tested for their ability to vaccinate against Her2-expressing tumors in two different in vivo models. Protection was assessed both against a lethal challenge with a BALB/c mammary carcinoma transfected with human Her2 (D2F2/E2) and against the outgrowth of autochthonous mammary carcinomas in BALB-neuT mice, transgenic for the activated rat Her2 oncogene. A single injection of Her2(1-683)PyVLPs before tumor inoculation induced a complete rejection of D2F2/E2 tumor cells in BALB/c mice. Similarly, a single injection of Her2(1-683)PyVLPs at 6 weeks of age protected BALB-neuT mice with atypical hyperplasia from a later outgrowth of mammary carcinomas, whereas all controls developed palpable tumors in all mammary glands. VLPs containing only VP1 and VP2 did not induce protection. The protection elicited by Her2(1-683)PyVLPs vaccination was most likely due to a cellular immune response because a Her2-specific response was shown in an ELISPOT assay, whereas antibodies against Her2 were not detected in any of the two models. The results show the feasibility of using MPyV-VLPs carrying Her2 fusion proteins as safe and efficient vaccines against Her2-expressing tumors.

Tags: Female
Descriptors: *Cancer Vaccines--immunology--IM; *Capsid Proteins --immunology--IM; *Mammary Neoplasms, Experimental--immunology--IM; *Mammary Neoplasms, Experimental--prevention and control--PC; *Receptor, erbB-2--immunology--IM; Animals; Antibodies, Viral--biosynthesis--BI; Antibodies, Viral--immunology--IM; Cancer Vaccines--genetics--GE; Cancer Vaccines--pharmacology--PD; Capsid Proteins--genetics--GE; Humans; Mice; Mice, Inbred BALB C; Neoplasm Transplantation; Polyomavirus--genetics--GE; Polyomavirus--immunology--IM; Rats; Receptor, erbB-2--biosynthesis--BI; Recombinant Fusion Proteins--genetics--GE; Recombinant Fusion Proteins --immunology--IM; Research Support, N.I.H., Extramural; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.; T-Lymphocytes --immunology--IM; Vaccination--methods--MT
CAS Registry No.: 0 (Antibodies, Viral); 0 (Cancer Vaccines); 0 (Capsid Proteins); 0 (Recombinant Fusion Proteins); 0 (VP1 protein, polyomavirus); 0 (VP2 protein, Polyomavirus)
Enzyme No.: EC 2.7.1.112 (Receptor, erbB-2)
Record Date Created: 20050704
Record Date Completed: 20050907

6/9/2 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0015788546 BIOSIS NO.: 200600133941
Vector prime-protein boost vaccine induces immune response against "self-antigens" associated with epithelial neoplasms and tumor vascular endothelial cells.
AUTHOR: Tang Yucheng (Reprint); Maynard Jonathan; Akbulut Hakan; Linton Phyllis-Jean; Deisseroth Albert B
AUTHOR ADDRESS: Sidney Kimmel Canc Ctr, Gene Therapy Program, San Diego, CA USA**USA
JOURNAL: Blood 106 (11, Part 2): p471B-472B NOV 16 2005 2005

CONFERENCE/MEETING: 47th Annual Meeting of the
American-Society-of-Hematology Atlanta, GA, USA December 10 -13, 2005;
20051210
SPONSOR: Amer Soc Hematol
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In order to develop a method to overcome the immune tolerance of cancer, we have designed an Ad-sig-TAA/ecdCD40L adenoviral vector vaccine for the in vivo activation and tumor antigen loading of dendritic cells (DCs). Subcutaneous (sc) injection of the Ad-sig-TAA/ecdCD40L adenoviral vector results in the secretion for 10 days from the vector infected cells of a fusion protein composed of a fragment of a tumor associated antigen (TAA) fused to the extracellular domain (ecd) of the CD40 ligand (CD40L). CD40L is a homotrimeric protein normally found on B cells and helper CD4(+)T cell lymphocytes. All of the sequences necessary to stabilize this trimeric structure of the protein are contained within the ecd of the CD40L protein. The binding of the TAA/ecdCD40L protein to DCs induces migration of these DCs to the regional lymph nodes. These DCs carry fragments of TAA bound to surface MHC Class I molecules. We have shown that the Ad-sig-TAA/ecdCD40L vector strategy can induce a cellular and humoral immune that persists for over a year indicating that a durable memory response is generated. We showed that sc injections of the Ad-sig-rH2N/ecdCD40L vector in rH2N.Tg mice induces a cellular and humoral immune response against the rat Her-2-Neu (rH2N) antigen which is associated with breast cancer. We showed that the sc injection of the Ad-sig-rH2N/ecdCD40L adenoviral vector in a rH2N.Tg transgenic mouse induced resistance to the growth of rH2N positive cancer cells in mice previously anergic to the rH2N antigen. We demonstrated that the sc injection of the Ad-sig-hMUC-1/ecdCD40L vector suppressed the growth of tumor cells positive for the human MUC-1 (hMUC-1) antigen in hMUC-1. Tg mice which were previously anergic to the hMUC-1 antigen. The sc injection of the Ad-sig-hMUC-1/ecdCD40L vector followed by sc injection of two booster injections of the hMUC-1/ecdCD40L protein induced high levels of hMUC-1 specific turner infiltrating effector CD8 positive T cells and hMUC-1 antibodies which bound to human breast and prostate cancer cells. In addition, we recently showed that the Ad-sig-TAA/ecdCD40L strategy could be used to activate a cellular and Immoral immune response against Annexin A1 (AnxA1), which is a marker uniquely displayed on the luminal membrane of tumor vascular endothelial cells but not on the luminal membrane of vascular endothelial cells of normal tissue. The subcutaneous injection of the Ad-sig-AnxA1/ecdCD40L vector suppressed the growth of AnxA1 negative tumor cells in a syngeneic mouse tumor model. This vector prime/protein boost vaccination was found to induce increased levels of effector CD8 positive T cells in the target tumor. These effector T cells were shown express increased levels of the genes encoding the CCR5 chemokine receptor and the CCL3 chemokine ligand which promote the infiltration of antigen specific effector T cells in the target tumor tissues. The response to cancer vaccines is often reduced in older individuals in part due to an intrinsic functional defect in CD4 cells. The Ad-sig-TAA/ecdCD40L vaccine may circumvent this defect because we have shown that the induction of the immune response is CD4 independent. These data suggest that this vector prime-protein boost vaccination strategy will be useful in the reduction of the frequency of recurrence following initial therapy for a wide variety of neoplastic diseases.

DESCRIPTORS:

MAJOR CONCEPTS: Molecular Genetics--Biochemistry and Molecular Biophysics ; Immune System--Chemical Coordination and Homeostasis
BIOSYSTEMATIC NAMES: Adenoviridae--dsDNA Viruses, Viruses, Microorganisms ; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: Adenovirus (Adenoviridae)--gene vector; mouse (Muridae)
ORGANISMS: PARTS ETC: lymphocyte--immune system, blood and lymphatics; B cell--immune system, blood and lymphatics; dendritic cell--immune system; CD4 positive T cell--immune system
COMMON TAXONOMIC TERMS: Double-Stranded DNA Viruses; Microorganisms; Viruses; Animals; Chordates; Mammals; Nonhuman Vertebrates; Nonhuman Mammals; Rodents; Vertebrates
CHEMICALS & BIOCHEMICALS: CD40 ligand {CD40L}; tumor associated antigen
METHODS & EQUIPMENT: gene delivery--laboratory techniques, genetic techniques
CONCEPT CODES:
00520 General biology - Symposia, transactions and proceedings
02506 Cytology - Animal
03502 Genetics - General
03506 Genetics - Animal
10064 Biochemistry studies - Proteins, peptides and amino acids
15002 Blood - Blood and lymph studies
15004 Blood - Blood cell studies
31500 Genetics of bacteria and viruses
33502 Virology - General and methods
34502 Immunology - General and methods
BIOSYSTEMATIC CODES:
03116 Adenoviridae
86375 Muridae

6/9/3 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

13741518 EMBASE No: 2006160896
HER-2/neu cancer vaccines: Present status and future prospects
Kaumaya P.T.P.
P.T.P. Kaumaya, 316 Tzagournis Medical Research Facility, 420 W12th Avenue, Columbus, OH 43210 United States
AUTHOR EMAIL: Kaumaya.1@osu.edu
International Journal of Peptide Research and Therapeutics (INT. J. PEPT. RES. THER.) (United States) 2006, 12/1 (65-77)
ISSN: 1573-3149 eISSN: 1573-3904
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 104

Immunotherapeutic approaches to cancer should focus on novel undertakings that modulate immune responses by synergistic enhancement of anti-tumor immunological parameters. Cancer vaccines should preferably be composed of multiple defined tumor antigen specific B- and T-cell epitopes. The main focus of this article is to briefly review the present status of Her-2/neu vaccine strategies and to describe the innovative strategies developed in my laboratory for a vaccine against HER-2/neu (ErbB-2) with emphasis on the humoral arm of the immune response. Elucidating the underlining mechanisms of anti-tumor effects elicited by peptide vaccines against a self-protein is a requirement for developing an immunotherapeutic strategy that might be effective in human cancer vaccines. Our approach entails the identification of biologically relevant epitopes, establishing relevant in vitro assays for monitoring vaccine efficacy, devising strategies to engineer

conformationally dependent sequences, developing highly immunogenic vaccines for an outbred population and delivering the immunogen/vaccine in a safe and efficacious vehicle, utilizing transgenic animal models for assessing tumor development, and developing challenge models using transplantable tumors to study efficacy of vaccine constructs. We have developed a multi-HER-2/neu B-cell epitope approach and shown in preclinical studies that immunization with a combination of two B-cell epitope was more effective in preventing mammary tumors than a single epitope. We have translated that work to the clinic (OSU 0105) in an FDA approved, NCI sponsored "Phase 1 Active Immunotherapy trial with Chimeric and Multi-epitope based peptide vaccine targeting HER-2 oncoprotein and nor-MDP adjuvant in patients with metastatic and/or recurrent solid tumors" at the James Cancer Hospital at the Ohio State University. The correlation between overexpression of HER-2/neu and up-regulation of VEGF has been demonstrated in breast cancer patients. Thus, blocking angiogenesis is an attractive strategy to inhibit tumor growth, invasion, and metastasis. The hypothesis that combination of anti-angiogenic therapy and tumor immunotherapy of cancer may be synergistic is an important future goal. In this review, I will discuss insights into our preclinical studies that might aid in the design of the next generation of cancer vaccines and become an integrated component of prophylactic/preventive and therapeutic approach. (c) 2006 Springer Science+Business Media, Inc.

DRUG DESCRIPTORS:
*epidermal growth factor receptor 2; *cancer vaccine--clinical trial--ct; * cancer vaccine--drug development--dv; *cancer vaccine--drug therapy--dt; * cancer vaccine--pharmaceutics--pr; *immunological adjuvant--pharmaceutics --pr; *peptide derivative--clinical trial--ct; *peptide derivative--drug development--dv; *peptide derivative--drug therapy--dt; *peptide derivative --pharmaceutics--pr; *peptide derivative--intraperitoneal drug administration--ip; *peptide derivative--subcutaneous drug administration --sc; *monoclonal antibody--clinical trial--ct; *monoclonal antibody--drug development--dv; *monoclonal antibody--drug therapy--dt; *monoclonal antibody--pharmacology--pd; *dendritic cell vaccine--drug development--dv epitope; trastuzumab--clinical trial--ct; trastuzumab--drug therapy--dt; trastuzumab--pharmacology--pd; antineoplastic agent--drug combination--cb; antineoplastic agent--drug therapy--dt; pertuzumab--clinical trial--ct; pertuzumab--drug therapy--dt; pertuzumab--pharmacology--pd; hybrid protein --drug development--dv; peptide antibody--drug development--dv; tumor cell vaccine--drug development--dv; bevacizumab--clinical trial--ct; bevacizumab --drug therapy--dt; bevacizumab--pharmacology--pd; protein tyrosine kinase inhibitor--clinical trial--ct; protein tyrosine kinase inhibitor--drug therapy--dt; vasculotropin receptor 2; receptor antibody--clinical trial --ct; receptor antibody--drug therapy--dt; unclassified drug
MEDICAL DESCRIPTORS:
*cancer--drug therapy--dt; *cancer--prevention--pc
antineoplastic activity; humoral immunity; drug efficacy; drug conformation ; immunogenicity; drug safety; cancer model; carcinogenesis; breast cancer; immunization; solid tumor; metastasis; protein expression; upregulation; tumor vascularization; cancer immunotherapy; cytotoxic T lymphocyte; human; nonhuman; clinical trial; review
DRUG TERMS (UNCONTROLLED): measles virus fusion protein--drug development --dv; triher 2 peptide--drug development--dv; triher 2 peptide --intraperitoneal drug administration--ip; triher 2 peptide--subcutaneous drug administration--sc; cyclopeptidic vasculotropin inhibitor--drug development--dv
CAS REGISTRY NO.: 137632-09-8 (epidermal growth factor receptor 2); 180288-69-1 (trastuzumab); 216974-75-3 (bevacizumab)
SECTION HEADINGS:
016 Cancer

026 Immunology, Serology and Transplantation
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

6/9/4 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

07815170 EMBASE No: 1999287254
Preparation and characterization of a recombinant humanized single- chain Fv antibody/human interleukin-2 fusion protein directed against the HER-2/neu (c-erbB2) proto-oncogene product, p185
Li J.; Gyorffy S.F.; Ring D.B.; Kwok C.S.; Austin R.C.
R.C. Austin, Hamilton Civic Hospitals Res. Centre, 711 Concession St., Hamilton, Ont. L8V 1C3 Canada
Tumor Targeting (TUMOR TARGETING) (United Kingdom) 1999, 4/2 (105-114)
CODEN: TUTAF ISSN: 1351-8488
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 35

High dose recombinant human interleukin 2 (rhIL-2) therapy has been used in the treatment of established tumors in both animal models and patients with advanced melanoma or renal carcinoma. However, because high dose rhIL-2 therapy causes severe systemic toxicity in normal tissues, its clinical use has been limited. Therefore, targeting interleukin-2 (IL-2) to the tumor site should improve its anti-tumor-immune response and decrease its systemic toxicity. In this study, we describe the preparation and characterization of a recombinant humanized single-chain Fv (sFv) antibody/IL-2 fusion protein. This recombinant fusion protein consists of humanized variable heavy (V(H)) and light (V(L)) domains of monoclonal antibody (mAb) 520C9 directed against the human HER-2/neu(c-erbB2) proto-oncogene product p185 and human IL-2. The fusion protein was stably expressed in baby hamster kidney cells and shown to retain the immunostimulatory activities of IL-2 as measured by IL-2-dependent cell proliferation and cytotoxicity assays. In addition to its IL-2 activity, this fusion protein also possesses binding specificity against the HER-2/neu (c-erbB2) proto-oncogene product, p185, as determined by enzyme linked immunosorbent assay (ELISA) using SKOV 3ip1 cells. Taken together, these findings suggest that this recombinant humanized sFv antibody/IL-2 fusion protein may provide an effective means of targeting therapeutic doses of IL- 2 to p185 positive tumors without increasing systemic toxicity or immunogenicity.

DRUG DESCRIPTORS:
*interleukin 2--drug therapy--dt; *interleukin 2--drug toxicity--to; * hybrid protein; *monoclonal antibody
MEDICAL DESCRIPTORS:
*oncogene neu; *proto oncogene; *protein analysis; *protein synthesis kidney carcinoma--drug therapy--dt; melanoma--drug therapy--dt; immune response; protein expression; cell proliferation; drug cytotoxicity; protein binding; drug targeting; binding affinity; nonhuman; controlled study; animal cell; article; priority journal
CAS REGISTRY NO.: 85898-30-2 (interleukin 2)
SECTION HEADINGS:
016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index

6/9/5 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

10254040 Genuine Article#: 503ZJ Number of References: 36
Title: Dendritic cell-based treatment of cancer: Closing in on a cellular therapy
Author(s): Valone FH (REPRINT) ; Small E; MacKenzie M; Burch P; Lacy M; Peshwa MV; Laus R
Corporate Source: 3005 1st Ave/Seattle//WA/98121 (REPRINT); Dendreon Corp,Seattle//WA/; Univ Calif San Francisco,San Francisco//CA/94143; Sacramento Med Fdn,Sacramento//CA/; Mayo Clin,Rochester//NY/
Journal: CANCER JOURNAL, 2001, V7, 2 (NOV-DEC), PS53-S61
ISSN: 1528-9117 Publication date: 20011100
Publisher: JONES AND BARTLETT PUBLISHERS, 40 TALL PONE DR, SUDBURY, MA 01776 USA
Language: English Document Type: ARTICLE
Geographic Location: USA
Journal Subject Category: ONCOLOGY
Abstract: PURPOSE Dendritic cells are the most potent antigen-presenting cells and are critical to initiation of immune responses. Dendritic cells loaded ex vivo with tumor-associated antigen are being administered to cancer patients in an effort to jump-start a potent, cell-mediated anticancer immune response resulting in tumor shrinkage and clinical benefit.

PATIENTS AND METHODS Dendreon Corporation has designed three therapeutic vaccines using blood-derived dendritic cells loaded ex vivo with antigen: Provenge (TM) for prostate cancer; Mylovenge (TM) for multiple myeloma and other B-cell malignancies; and APC8024 for cancers expressing the HER-2/neu proto-oncogene.

RESULTS Preclinical studies demonstrated that blood dendritic cells matured spontaneously in short-term culture without growth factors, and that fusion of antigens with granulocyte-macrophage colony-stimulating factor enhances antigen uptake and presentation by blood dendritic cells. Phase I/II trials suggest that these dendritic cell-based vaccines are safe and well tolerated. Provenge has demonstrated antitumor activity in hormone-refractory prostate cancer; approximately 20% of patients experienced decreased prostate-specific antigen (i.e., PSA) levels and a similar percentage experienced disease stabilization. Double-blind, placebo-controlled, randomized trials in metastatic, asymptomatic hormone-refractory prostate cancer have been initiated. Phase II data on Mylovenge are similarly encouraging, and expanded phase II testing is ongoing in anticipation of opening phase III trials in 2002. APC8024 is in early clinical development and has shown significant capacity to elicit antigen-specific immune responses.

CONCLUSION Antigen delivery by ex-vivo antigen-loaded dendritic cells may be an effective approach to cancer immunotherapy.
Descriptors--Author Keywords: dendritic cells ; antigen presenting cells ; prostate ; myeloma ; prostatic acid phosphatase ; HER-2/neu
Identifiers--KeyWord Plus(R): PROSTATE-CANCER; PHASE-I; MELANOMA PATIENTS; MULTIPLE-MYELOMA; TUMOR-IMMUNITY; FUSION PROTEIN; VACCINATION; ANTIGEN; IMMUNOTHERAPY; INDUCTION
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6/9/6 (Item 2 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06599838 Genuine Article#: ZD573 Number of References: 45

Title: A B7.1-antibody fusion protein retains antibody specificity and ability to activate via the T cell costimulatory pathway

Author(s): ChallitaEid PM; Penichet ML; Shin SU; Poles T; Mosammaparast N; Mahmood K; Slamon DJ; Morrison SL; Rosenblatt JD (REPRINT)
Corporate Source: UNIV ROCHESTER,CTR CANC, HEMATOL ONCOL UNIT, 601 ELMWOOD AVE, BOX 704/ROCHESTER//NY/14642 (REPRINT); UNIV ROCHESTER,CTR CANC, HEMATOL ONCOL UNIT/ROCHESTER//NY/14642; UNIV ROCHESTER,DEPT MICROBIOL & IMMUNOL/ROCHESTER//NY/14642; UNIV CALIF LOS ANGELES,INST MOL BIOL, DEPT MICROBIOL & MOL GENET/LOS ANGELES//CA/90095; UNIV CALIF LOS ANGELES,DEPT MED, DIV HEMATOL ONCOL/LOS ANGELES//CA/90095; HALLYM UNIV,INST ENVIRONM & LIFE SCI/KANGWAN DO//SOUTH KOREA/
Journal: JOURNAL OF IMMUNOLOGY, 1998, V160, N7 (APR 1), P3419-3426
ISSN: 0022-1767 Publication date: 19980401
Publisher: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814
Language: English Document Type: ARTICLE
Geographic Location: USA; SOUTH KOREA
Subfile: CC LIFE--Current Contents, Life Sciences
Journal Subject Category: IMMUNOLOGY
Abstract: We describe the construction and characterization of an Ab fusion protein specific for the tumor-associated Ag HER2/neu linked to sequences encoding the extracellular domain of the B7.1 T cell

costimulatory ligand, The Ab domain of the fusion molecule will specifically target HER2/neu-expressing tumor cells, while the B7.1 domain is designed to activate a specific immune response, We show that the B7.1 fusion Ab retained ability to selectively bind to the HER2/neu Ag and to the CTLA4/CD28 counter-receptors for B7.1, Specific T cell activation was observed when the B7.1 Ab fusion protein was bound to HER2/neu-expressing cells, The use of the B7.1 Ab fusion protein may overcome limitations of gene transfer and/or standard Ab therapy and represents a novel approach to the eradication of minimal residual disease.

Identifiers--KeyWord Plus(R): HER-2 NEU ONCOGENE; BREAST-CANCER; ANTITUMOR IMMUNITY; TUMOR-IMMUNITY; B7; EXPRESSION; MOLECULES; CHEMOTHERAPY; INDUCTION; BINDING

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Set     Items   Description
S1     519033   ((ERB (N) B2) OR (HER (N) 2) AND CHIMERA OR FUSION)
S2      16318   (ERB (N) B2) OR (HER (N) 2)
S3        107   S2 AND (FUSION (N) PROTEIN)
S4         57   RD S3  (unique items)
S5          6   (IMMUNE (N) RESPONSE) AND S4
S6          6   RD S5  (unique items)
?

S S2 AND CHIMER?
          16318  S2
         162781  CHIMER?
      S7    158  S2 AND CHIMER?
?

RD S7
      S8     84  RD S7  (unique items)
?


Set     Items   Description
S1     519033   ((ERB (N) B2) OR (HER (N) 2) AND CHIMERA OR FUSION)
S2      16318   (ERB (N) B2) OR (HER (N) 2)
S3        107   S2 AND (FUSION (N) PROTEIN)
S4         57   RD S3  (unique items)
S5          6   (IMMUNE (N) RESPONSE) AND S4
S6          6   RD S5  (unique items)
S7        158   S2 AND CHIMER?
S8         84   RD S7  (unique items)
?

S S8 AND (IMMUNE (N) RESPONSE)
             84  S8
        2489021  IMMUNE
        4806444  RESPONSE
         358922  IMMUNE(N)RESPONSE
      S9      5  S8 AND (IMMUNE (N) RESPONSE)
?

RD S9
     S10      5  RD S9  (unique items)
?

TYPE S10/FULL/1-5

  10/9/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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20845306   PMID: 16730262
 Development of antibodies and chimeric molecules for cancer
 immunotherapy.
  Waldmann Thomas A; Morris John C
  Metabolism Branch, Center for Cancer Research, National Cancer Institute
NIH, Bethesda, Maryland 20892, USA.
  Advances in immunology (United States)     2006,  90   p83-131,  ISSN
0065-2776--Print   Journal Code: 0370425
  Publishing Model Print
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Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process
Subfile: INDEX MEDICUS

Monoclonal antibodies are among the most rapidly expanding class of therapeutics for cancer treatment. Monoclonal antibodies targeting non-Hodgkin's lymphoma (NHL), Her-2/neu highly expressing metastatic breast cancer, colorectal cancer, acute myelogenous leukemia, and B-cell chronic lymphocytic leukemia (CLL) have received FDA approval. Promising new targets for antibody therapy include cellular growth factor receptors, mediators of tumor-driven neo-angiogenesis, as well as host negative immunoregulatory checkpoints that impede an effective immune response to neoplasia. Antibody efficacy has been increased by genetic engineering to humanize the antibodies and to increase their effector functions including antibody dependent cellular cytotoxicity. Furthermore, antibodies have been armed with cytokines, chemotherapeutic agents, toxins, and radionuclides to augment their efficacy as tumor cytotoxic agents. As a consequence of these advances, 30 years after their first development, monoclonal antibodies have become an important standard approach for the therapy of neoplasia with 19 therapeutic monoclonal antibodies now approved by the FDA including 8 for the treatment of cancer.

Record Date Created: 20060529

10/9/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13405904 PMID: 11580228
The N-terminal flanking region of the invariant chain peptide augments the immunogenicity of a cryptic "self" epitope from a tumor-associated antigen.

Hess A D; Thoburn C; Chen W; Miura Y; Van der Wall E

Division of Immunology and Hematopoiesis, Department of Oncology, The Johns Hopkins University, Bunting and Blaustein Cancer Research Building, Baltimore, Maryland 21231, USA.

Clinical immunology (Orlando, Fla.) (United States) Oct 2001, 101 (1) p67-76, ISSN 1521-6616--Print Journal Code: 100883537

Contract/Grant No.: AI 24319; AI; NIAID; CA 15396; CA; NCI; CA 82583; CA; NCI

Publishing Model Print; Erratum in Clin Immunol 2001 Dec;101(3) 381

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

The N-terminal flanking region of the invariant chain peptide termed CLIP appears to have superagonistic properties interacting with the T cell receptor and the MHC class II molecule at or near the binding site for the bacterial superantigen Staphylococcal enterotoxin B (SEB). The present studies explored the hypothesis that the N-terminal segment of CLIP can augment the immunogenicity of cryptic "self" tumor-associated antigens. A chimeric construct of an MHC class II binding peptide from the c-erb oncogene (Her-2/neu) containing the N-terminal flanking region of CLIP elicited potent antitumor activity against a Her-2/neu-positive tumor in a rat model system. Comparatively, the unmodified parent peptide was ineffective. The induction of effective antitumor immunity, however, required presentation of the chimeric peptide construct on irradiated tumor cells or the peptide construct in concert with a Her-2/neu MHC class

I-restricted peptide from Her-2/neu. As revealed by adoptive transfer studies, effective protective antitumor immunity in this setting required the CD4 T helper subset. Additionally, in vitro analysis revealed that immunization with the parent peptide resulted in a weak immune response to the unmodified peptide consisting of both type 1 (IL-2, IFN-gamma) and type 2 (IL-4, IL-10) cytokine-producing cells analyzed by RT-PCR (qualitative and quantitative) and by limiting dilution assay. Comparatively, immunization with the chimeric construct elicited a potent immune response to the parent peptide with predominantly type 1 cytokine-producing cells. Taken together, the results suggest that immunization with the chimeric Her-2/neu peptide induced protective antitumor immunity. Associated with this immunization strategy was the enhancement of a type 1 cytokine response. Copyright 2001 Academic Press.

Descriptors: *Antigens, Differentiation, B-Lymphocyte--chemistry--CH; *Antigens, Differentiation, B-Lymphocyte--physiology--PH; *Antigens, Neoplasm--immunology--IM; *Cancer Vaccines; *Histocompatibility Antigens Class II--chemistry--CH; *Histocompatibility Antigens Class II--physiology --PH; *Neoplasms, Experimental--immunology--IM; *Peptide Fragments --immunology--IM; Animals; Antigens, Differentiation, B-Lymphocyte --genetics--GE; Antigens, Neoplasm--genetics--GE; Cells, Cultured; Cytokines--biosynthesis--BI; Dendritic Cells--transplantation--TR; Epitopes --immunology--IM; Histocompatibility Antigens Class II--genetics--GE; Immunotherapy, Adoptive; Neoplasms, Experimental--therapy--TH; Rats; Rats, Inbred F344; Receptor, erbB-2--genetics--GE; Receptor, erbB-2--immunology --IM; Recombinant Fusion Proteins--immunology--IM; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.; Survival Rate; T-Lymphocytes, Cytotoxic--immunology--IM; Th1 Cells--immunology--IM; Tumor Cells, Cultured

CAS Registry No.: 0 (Antigens, Differentiation, B-Lymphocyte); 0 (Antigens, Neoplasm); 0 (Cancer Vaccines); 0 (Cytokines); 0 (Epitopes); 0 (Histocompatibility Antigens Class II); 0 (Peptide Fragments); 0 (Recombinant Fusion Proteins); 0 (invariant chain)

Enzyme No.: EC 2.7.1.112 (Receptor, erbB-2)

Record Date Created: 20011002

Record Date Completed: 20011204

10/9/3 (Item 1 from file: 35)

DIALOG(R)File 35:Dissertation Abs Online

01830981 ORDER NO: AADAA-I3011042

Evaluation of chimeric B-cell epitope vaccines of HER-2: Application to cancer patients

Author: Dakappagari, Naveen K.

Degree: Ph.D.

Year: 2001

Corporate Source/Institution: The Ohio State University (0168)

Adviser: Pravin T. P. Kaumaya

Source: VOLUME 62/04-B OF DISSERTATION ABSTRACTS INTERNATIONAL. PAGE 1795. 175 PAGES

Descriptors: HEALTH SCIENCES, IMMUNOLOGY ; HEALTH SCIENCES, ONCOLOGY

Descriptor Codes: 0982; 0992

ISBN: 0-493-21040-7

Overexpression of Human Epidermal growth factor Receptor-2 (HER-2) causes cellular transformation in experimental models. About 30% of carcinoma patients manifest HER-2 overexpression, which is associated with poor clinical prognosis and resistance to conventional forms of cancer therapy. Amplified expression of HER-2 activates host immune response

during early stages of cancer, however the natural immune responses are too low to control tumor progression. Passive therapy with HER-2 specific monoclonal antibodies produced objective responses in about 20% of receptor positive patients. Active specific immunotherapy offers the possibility for generating sustained antitumor responses and is potentially more beneficial than passive therapy. The main goal of this study was to develop a vaccine strategy that can elicit an effective immune response in an outbred population capable of inhibiting the growth of HER-2 associated cancer. This goal was addressed by an incremental approach. First synthetic peptides corresponding to the Bell epitopes of HER 2 were evaluated for their ability to produce high levels of antibodies reactive with native receptor. Second, the antitumor activity of the peptide antibodies were tested on cancer cell proliferation in culture and on tumors induced in mice. Third, a combination of selected B-cell epitope peptides was evaluated for synergistic growth inhibition. Fourth, the potential of supplemental immunization with cytokines to enhance the immunogenicity and antitumor activity of the peptide epitopes was assessed. In addition, the molecular mechanisms of peptide antibody-mediated tumor growth inhibition were investigated. Attempts were made to stabilize the conformation of the B-cell epitopes to elicit high affinity antibodies. A total of nine HER-2 B-cell epitopes were synthesized as chimeras with a promiscuous T-helper epitope derived from Measles Virus Fusion (MVF) protein. Following initial evaluation of four chimeric peptides, one candidate, MVF HER-2 [628-647] was identified that selectively inhibited growth of cancer cells <italic> in vitro</italic> and prevented spontaneous tumor development in HER-2/neu transgenic mice. Three of the five cancer patients immunized with MVF HER-2 [628-647] elicited antibodies capable of killing breast cancer cells in culture. Further analyses lead to the identification of two more epitopes, 316-339 and 485-503, antibodies against which inhibited tumor cell proliferation. Immunization with a combination of 316-339 and 628-647 elicited antibodies with the best growth inhibitory activities. Supplemental immunization with interleukin-12 elicited significantly higher levels of antibodies to both single and a combination of chimeric peptides in addition to inducing antibody subtypes (e.g. IgG2a) that have been described to kill tumor cells more efficiently. Significant reduction of lung metastases was observed in mice vaccinated with peptide 316-339 alone or a combination of peptides, 316-339 and 628-647 plus IL-12. Based on these results, the combination of two peptides, 316-339 and 628-647 has been approved for testing in human cancer patients. Antibodies induced by peptide vaccines inhibit tumor growth by multiple mechanisms including down modulation of cell surface receptor, release of interferon-γ and lysis of tumor cells in presence of mononuclear cells.

10/9/4 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

13741518 EMBASE No: 2006160896
HER-2/neu cancer vaccines: Present status and future prospects
Kaumaya P.T.P.
P.T.P. Kaumaya, 316 Tzagournis Medical Research Facility, 420 W12th Avenue, Columbus, OH 43210 United States
AUTHOR EMAIL: Kaumaya.1@osu.edu
International Journal of Peptide Research and Therapeutics (INT. J. PEPT. RES. THER.) (United States) 2006, 12/1 (65-77)
ISSN: 1573-3149 eISSN: 1573-3904
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 104

Immunotherapeutic approaches to cancer should focus on novel undertakings that modulate immune responses by synergistic enhancement of anti-tumor immunological parameters. Cancer vaccines should preferably be composed of multiple defined tumor antigen specific B- and T-cell epitopes. The main focus of this article is to briefly review the present status of Her-2/neu vaccine strategies and to describe the innovative strategies developed in my laboratory for a vaccine against HER-2/neu (ErbB-2) with emphasis on the humoral arm of the immune response. Elucidating the underlining mechanisms of anti-tumor effects elicited by peptide vaccines against a self-protein is a requirement for developing an immunotherapeutic strategy that might be effective in human cancer vaccines. Our approach entails the identification of biologically relevant epitopes, establishing relevant in vitro assays for monitoring vaccine efficacy, devising strategies to engineer conformationally dependent sequences, developing highly immunogenic vaccines for an outbred population and delivering the immunogen/vaccine in a safe and efficacious vehicle, utilizing transgenic animal models for assessing tumor development, and developing challenge models using transplantable tumors to study efficacy of vaccine constructs. We have developed a multi-HER-2/neu B-cell epitope approach and shown in preclinical studies that immunization with a combination of two B-cell epitope was more effective in preventing mammary tumors than a single epitope. We have translated that work to the clinic (OSU 0105) in an FDA approved, NCI sponsored "Phase 1 Active Immunotherapy trial with Chimeric and Multi-epitope based peptide vaccine targeting HER-2 oncoprotein and nor-MDP adjuvant in patients with metastatic and/or recurrent solid tumors" at the James Cancer Hospital at the Ohio State University. The correlation between overexpression of HER-2/neu and up-regulation of VEGF has been demonstrated in breast cancer patients. Thus, blocking angiogenesis is an attractive strategy to inhibit tumor growth, invasion, and metastasis. The hypothesis that combination of anti-angiogenic therapy and tumor immunotherapy of cancer may be synergistic is an important future goal. In this review, I will discuss insights into our preclinical studies that might aid in the design of the next generation of cancer vaccines and become an integrated component of prophylactic/preventive and therapeutic approach. (c) 2006 Springer Science+Business Media, Inc.

DRUG DESCRIPTORS:
*epidermal growth factor receptor 2; *cancer vaccine--clinical trial--ct; * cancer vaccine--drug development--dv; *cancer vaccine--drug therapy--dt; * cancer vaccine--pharmaceutics--pr; *immunological adjuvant--pharmaceutics --pr; *peptide derivative--clinical trial--ct; *peptide derivative--drug development--dv; *peptide derivative--drug therapy--dt; *peptide derivative --pharmaceutics--pr; *peptide derivative--intraperitoneal drug administration--ip; *peptide derivative--subcutaneous drug administration --sc; *monoclonal antibody--clinical trial--ct; *monoclonal antibody--drug development--dv; *monoclonal antibody--drug therapy--dt; *monoclonal antibody--pharmacology--pd; *dendritic cell vaccine--drug development--dv epitope; trastuzumab--clinical trial--ct; trastuzumab--drug therapy--dt; trastuzumab--pharmacology--pd; antineoplastic agent--drug combination--cb; antineoplastic agent--drug therapy--dt; pertuzumab--clinical trial--ct; pertuzumab--drug therapy--dt; pertuzumab--pharmacology--pd; hybrid protein --drug development--dv; peptide antibody--drug development--dv; tumor cell vaccine--drug development--dv; bevacizumab--clinical trial--ct; bevacizumab --drug therapy--dt; bevacizumab--pharmacology--pd; protein tyrosine kinase inhibitor--clinical trial--ct; protein tyrosine kinase inhibitor--drug therapy--dt; vasculotropin receptor 2; receptor antibody--clinical trial --ct; receptor antibody--drug therapy--dt; unclassified drug
MEDICAL DESCRIPTORS:

*cancer--drug therapy--dt; *cancer--prevention--pc
antineoplastic activity; humoral immunity; drug efficacy; drug conformation ; immunogenicity; drug safety; cancer model; carcinogenesis; breast cancer; immunization; solid tumor; metastasis; protein expression; upregulation; tumor vascularization; cancer immunotherapy; cytotoxic T lymphocyte; human; nonhuman; clinical trial; review
DRUG TERMS (UNCONTROLLED): measles virus fusion protein--drug development --dv; triher 2 peptide--drug development--dv; triher 2 peptide --intraperitoneal drug administration--ip; triher 2 peptide--subcutaneous drug administration--sc; cyclopeptidic vasculotropin inhibitor--drug development--dv
CAS REGISTRY NO.: 137632-09-8 (epidermal growth factor receptor 2); 180288-69-1 (trastuzumab); 216974-75-3 (bevacizumab)
SECTION HEADINGS:
016 Cancer
026 Immunology, Serology and Transplantation
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

10/9/5 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

14492723 Genuine Article#: 977LK Number of References: 163
Title: T cell avidity and tumor recognition: implications and therapeutic strategies
Author(s): McKee MD (REPRINT) ; Roszkowski JJ; Nishimura MI
Corporate Source: Univ Chicago,Dept Surg,5841 S Maryland Ave/Chicago//IL/60637 (REPRINT); Univ Chicago,Dept Surg,Chicago//IL/60637(mmckee@surgery.bsd.uchicago.edu; jroszkow@surgery.bsd.uchicago.edu; mnishimu@surgery.bsd.uchicago.edu)
Journal: JOURNAL OF TRANSLATIONAL MEDICINE, 2005, V3 (SEP 20), P1-12, 35
ISSN: 1479-5876 Publication date: 20050920
Publisher: BIOMED CENTRAL LTD, MIDDLESEX HOUSE, 34-42 CLEVELAND ST, LONDON W1T 4LB, ENGLAND
Language: English Document Type: REVIEW
Geographic Location: USA
Journal Subject Category: MEDICINE, RESEARCH & EXPERIMENTAL
Abstract: In the last two decades, great advances have been made studying the immune response to human tumors. The identification of protein antigens from cancer cells and better techniques for eliciting antigen specific T cell responses in vitro and in vivo have led to improved understanding of tumor recognition by T cells. Yet, much remains to be learned about the intricate details of T cell - tumor cell interactions. Though the strength of interaction between T cell and target is thought to be a key factor influencing the T cell response, investigations of T cell avidity, T cell receptor (TCR) affinity for peptide-MHC complex, and the recognition of peptide on antigen presenting targets or tumor cells reveal complex relationships. Coincident with these investigations, therapeutic strategies have been developed to enhance tumor recognition using antigens with altered peptide structures and T cells modified by the introduction of new antigen binding receptor molecules. The profound effects of these strategies on T cell - tumor interactions and the clinical implications of these effects are of interest to both scientists and clinicians. In recent years, the focus of much of our work has been the avidity and effector characteristics of tumor reactive T cells. Here we review concepts and current results in the field, and the implications of therapeutic strategies using altered antigens and altered effector T

cells.
Identifiers--KeyWord Plus(R): LYMPH-NODE LYMPHOCYTES; CHIMERIC RECEPTOR GENE; CANCER-TESTIS ANTIGENS; HUMAN RENAL-CELL; WILD-TYPE P53; INFILTRATING LYMPHOCYTES; HUMAN-MELANOMA; SINGLE-CHAIN; IN-VITRO; HER-2/NEU PROTOONCOGENE
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L1        5681 (ERB B2) OR (HER 2)

=> s (fusion protein) and l1
L2         153 (FUSION PROTEIN) AND L1

=> s (immune response) and l2
L3          40 (IMMUNE RESPONSE) AND L2

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L4   ANSWER 1 OF 25  CAPLUS  COPYRIGHT 2006 ACS on STN DUPLICATE 1
AN   2006:317271  CAPLUS
DN   144:368350
TI   Listeria-based vaccines comprising fusion proteins of
     listeriolysin with CD8+ T cell epitope of antigen or tumor antigen
IN   Paterson, Yvonne; Singh, Reshma
PA   Trustess of the University of Pennsylvania, USA
SO   PCT Int. Appl., 104 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 5
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
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PI   WO 2006036550        A2    20060406    WO 2005-US32682         20050914
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             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
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             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
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KG, KZ, MD, RU, TJ, TM

	US 2005129715	A1	20050616	US 2004-949667	20040924
	US 2006093582	A1	20060504	US 2005-223945	20050913
PRAI	US 2004-949667	A	20040924		
	US 2005-223945	A	20050913		
	US 1994-336372	A2	19941108		
	US 2000-535212	A1	20000327		
	US 2003-441851	A2	20030520		

AB This invention provides methods of treating and vaccinating against an antigen-expressing tumor and inducing an immune response against a sub-dominant epitope of antigen, comprising a fusion of an listeriolysin fragment to the antigen or a recombinant Listeria strains (e.g. Listeria monocytogenes) expressing the antigen. The present invention also provides recombinant peptides comprising a listeriolysin (LLO) protein fragment used to a Her-2 protein or fragment thereof, recombinant Listeria strains expressing a Her-2 protein, vaccines and immunogenic compns. comprising same, and methods of inducing an Her-2 immune response and treating and vaccinating against a Her-2-expressing tumor, comprising same.

L4 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:409876 CAPLUS
DN 144:431116
TI Listeria-based vectors and listeriolysin O fusion protein-based tumor vaccines
IN Paterson, Yvonne; Singh, Reshma
PA Trustees of the University of Pennsylvania, USA
SO U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of U.S. Ser. No. 949,667.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2006093582	A1	20060504	US 2005-223945	20050913
	US 2005129715	A1	20050616	US 2004-949667	20040924
	WO 2006036550	A2	20060406	WO 2005-US32682	20050914

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI	US 2004-949667	A2	20040924		
	US 1994-336372	A2	19941108		
	US 2000-535212	A1	20000327		
	US 2003-441851	A2	20030520		
	US 2005-223945	A	20050913		

AB The authors disclose methods of vaccinating against an antigen-expressing tumor and inducing an immune response against a sub-dominant epitope of a tumor antigen. The methods comprise (i) a fusion of a listeriolysin (LLO) fragment to the antigen or (ii) a recombinant Listeria strain expressing the antigen. In one example, a breast tumor vaccine was constructed from an LLO fragment fused to an extracellular fragment of the Her-2 protein.

L4 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2

AN 2005:527197 CAPLUS
DN 143:58502
TI Listeria vaccine strain expressing chimeric protein of tumor antigen and truncated LLO protein for immunotherapy of cancer
IN Paterson, Yvonne; Singh, Reshma
PA The Trustees of the University of Pennsylvania, USA
SO U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U.S. Ser. No. 441,851.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005129715	A1	20050616	US 2004-949667	20040924
	US 6051237	A	20000418	US 1994-336372	19941108
	US 6565852	B1	20030520	US 2000-535212	20000327
	US 2003202985	A1	20031030	US 2003-441851	20030520
	US 2006093582	A1	20060504	US 2005-223945	20050913
	WO 2006036550	A2	20060406	WO 2005-US32682	20050914

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI	US 1994-336372	A2	19941108
	US 2000-535212	A1	20000327
	US 2003-441851	A2	20030520
	US 2004-949667	A2	20040924
	US 2005-223945	A	20050913

AB The present invention includes compns., methods and kits for inducing an immune response to a tumor and for treating cancer with a Listeria vaccine strain expressing an antigen fused to a truncated listeriolysin O or LLO protein. The Listeria vaccine strain is Listeria monocytogenes. The tumor antigen is Her-2/neu or fragment, bcr/abl, HPV E6 or E7, MZ2-E, MAGE-1 or MVC-1. The vaccine is for treating cancer in mammal and human.

L4 ANSWER 4 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2005-21518 BIOTECHDS
TI Generating immune response against antigen e.g. tumor antigen, comprises administering expression vector comprising transcription unit encoding secretable fusion protein having antigen and CD40 ligand, and fusion protein, to individual;
involving vector-mediated gene transfer and expression in host cell for recombinant vaccine preparation
AU DIESSEROTH A; TANG Y; ZHANG W; FANG X
PA KIMMEL CANCER CENT SIDNEY
PI WO 2005058950 30 Jun 2005
AI WO 2004-US41690 10 Dec 2004
PRAI US 2003-592016 11 Dec 2003; US 2003-592016 11 Dec 2003
DT Patent
LA English
OS WPI: 2005-488540 [49]
AN 2005-21518 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Generating (M1) an immune response in an

individual against an antigen, comprising administering to the individual an expression vector comprising a transcription unit encoding a secretable fusion protein, comprising the antigen and CD40 ligand, and administering a fusion protein comprising the antigen and CD40 ligand, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) treating (M2) an individual with cancer that expresses a tumor antigen; (2) generating (M3) immunity in a subject to an infectious agent; (3) simultaneous production (M4) of an expression vector that encodes a fusion protein and the fusion protein ; and (4) a protein comprising a transcription unit encoding a secretable fusion protein having the antigen and CD40 ligand.

BIOTECHNOLOGY - Preparation: (M4) comprises culturing the cells containing the expression vector where the cells replicate the vector and produce the protein expressed from the vector into the culture medium during propagation. Preferred Method: In (M1), the transcription unit encodes a linker between the antigen and the CD40 ligand. The vector includes a human cytomegalovirus promoter/enhancer for controlling transcription of the transcription unit. The vector is a viral vector. The viral vector is an adenoviral vector. The CD40 ligand is human CD40 ligand. The CD40 ligand lacks a cytoplasmic domain. The vector encodes a CD40L that include no more than six residues from either end of the transmembrane domain. The vector does not encode the transmembrane domain of CD40 ligand. The CD40 ligand is missing all or substantially all of its transmembrane domain. The CD40 ligand comprises residues 47-261. The CD40 ligand comprises residues 1-23 and 47-261. The vector is rendered non-replicating in normal human cells. (M1) involves repeating the step of administering a fusion protein at a later time. The immune response includes the generation of cytotoxic CD8+T cells against the antigen or antibodies against the antigen. The sequence of CD40 ligand encoded by the vector and the sequence of CD40 ligand administered as a fusion protein are different. The sequence of the antigen encoded by the vector and the sequence of the antigen administered as a fusion protein are different. The transcription unit encodes a secretory signal sequence. The antigen is not from CD40 ligand.

ACTIVITY - Cytostatic; Virucide; Antibacterial; Fungicide; Protozoacide; Immunostimulant. The tumor suppression was tested as follows. Three combinations of Ad-sig-ecdhMUC-1/ecdCD40L vector and ecdhMUC-1/ecdCD40L protein were administered to hMUC-1.Tg mice before challenge with LL2/LL1hMUC-1 tumor cells. The successive vector injection (VVV) was given as three Ad-sig-ecdhMUC-1/DeltaCtDeltaTM CD40L vector subcutaneous injections administered on days 1, 7 and 21, the successive protein injection (PPP) was given as three ecdhMUC-1/DeltaCtDeltaTm CD40L protein subcutaneous injections administered on days 1, 7 and 21, or one vector and two protein injections (VPP) was given as a single Ad-sig-ecdhMUC-1/DeltaCtDeltaTm CD40L vector subcutaneous injection followed at days 7 and 21 by ecdhMUC-1/DeltaCtDeltaTm CD40L protein subcutaneous injections. The mice were challenged one week later with a subcutaneous injection of five hundred thousand LL2/LL1hMUC-1 lung cancer cells, and two weeks later with an intravenous injection of 500000 LL2/LL1hMUC-1 tumor cells. The size of the subcutaneous tumor nodules at day were measured by calliper at multiple time points to determine the effect of the various vaccine schedules on the growth of the LL2/LL1hMUC-1 cells as subcutaneous nodules. The metastases were measured by total lung weight following sacrifice. Results showed that three injections of the fusion protein (PPP) without a preceding Ad-sig-ecdhMUC-1/ecdCD40L vector injection failed to induce complete resistance to the development of the subcutaneous LL2/LL1hMUC-1 tumor. In contrast, the schedule of VVV or VPP completely suppressed the appearance of the subcutaneous LL2/LL1hMUC-1 tumor.

MECHANISM OF ACTION - Vaccine.

USE - (M1) is useful for generating an immune response in an individual against an antigen. The antigen is a

polypeptide antigen or an infectious agent antigen. The immune response is directed against a cell expressing the antigen or directed against a microorganism expressing the antigen. The antigen is a tumor antigen. The tumor antigen is from HER-2 or a mucin such as MUC1, MUC2, MUC3A, MUC3B, MUC4, MUC5AC, MUC5B, MUC6, MUC7, MUC8, MUC9, MUC12, MUC13, MUC15 or MUC16, preferably MUC1. The mucin antigen comprises the extracellular domain of a mucin, preferably MUC1. The mucin antigen comprises at least one tandem repeat of a mucin. The antigen is a self antigen in the individual. The antigen is E7 protein of human papilloma virus. The antigen is from epithelial cancer cells. The methods are useful for treating an individual with cancer that expresses a tumor antigen, and for generating immunity in a subject to an infectious agent. The infectious agent antigen is chosen from a viral antigen, bacterial antigen, fungal antigen and protozoan antigen. The infectious agent antigen is viral antigen. The viral antigen is the E6 or E7 protein of human papilloma virus (all claimed).

ADMINISTRATION - The fusion protein is administered after administration of the vector. The fusion protein is administered with an adjuvant, subcutaneously (claimed). The vector is administered intravascularly, intravenously, intraarterially, intramuscularly, orally, nasally, rectally, transdermally or by inhalation, at a dose of 1x107-1x1011, preferably 5x108-2x1010.

EXAMPLE - No relevant example is given.(65 pages)

L4 ANSWER 5 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2005-28914 BIOTECHDS
TI Generating an immune response against an antigen, comprises administering a vector comprising a transcription unit encoding a secretable fusion protein comprising the antigen and CD40 ligand;
involving adeno virus vector-mediated HER-2 tumor antigen gene transfer and expression in host cell for therapy and recombinant vaccine preparation
AU DEISSEROTH A; TANG Y; ZHANG W; FANG X
PA KIMMEL CANCER CENT SIDNEY
PI US 2005226888 13 Oct 2005
AI US 2004-9533 10 Dec 2004
PRAI US 2004-9533 10 Dec 2004; US 2003-529016 11 Dec 2003
DT Patent
LA English
OS WPI: 2005-683722 [70]
AN 2005-28914 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Generating an immune response in an individual against an antigen comprises administering an expression vector comprising a transcription unit encoding a secretable fusion protein, comprising the antigen and CD40 ligand, and administering the fusion protein.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a method of treating an individual with cancer that expresses a tumor antigen; (2) a method of generating immunity in a subject to an infectious agent; (3) a method of simultaneously producing an expression vector that encodes a fusion protein and the fusion protein; and (4) a protein comprising a transcription unit encoding a secretable fusion protein, comprising the antigen and CD40 ligand.

BIOTECHNOLOGY - Preferred Method: Generating an immune response in an individual against an antigen comprises administering an expression vector comprising a transcription unit encoding a secretable fusion protein, comprising the antigen and CD40 ligand and administering the fusion protein. The protein is administered after administration of the vector. The antigen is a polypeptide antigen. The antigen is an

infectious agent antigen. The immune response is directed against a cell expressing the antigen. The immune response is directed against a microorganism expressing the antigen. The antigen is a tumor antigen. The tumor antigen is from HER-2. The tumor antigen is a mucin. The tumor antigen is a mucin consisting of MUC1, MUC2, MUC3A, MUC3B, MUC4, MUC5AC, MUC5B, MUC6, MUC7, MUC8, MUC9, MUC12, MUC13, MUC15 or MUC16. The mucin antigen is MUC1. The mucin antigen comprises the extracellular domain of a mucin. The mucin antigen comprises at least one tandem repeat of a mucin. The mucin antigen comprises is the extracellular domain of MUC1. The antigen is a self-antigen in the individual. The antigen is the E7 protein of human papilloma virus. The antigen is from epithelial cancer cells. The transcription unit encodes a linker between the antigen and the CD40 ligand. The vector includes a human cytomegalovirus promoter/enhancer for controlling transcription of the transcription unit. The vector is a viral vector. The viral vector is an adenoviral vector. The CD40 ligand is human CD40 ligand. The CD40 ligand lacks a cytoplasmic domain. The vector encodes a CD40L that includes no more than six residues from either end of the transmembrane domain. The vector does not encode the transmembrane domain of CD40 ligand. The CD40 ligand is missing all or substantially all of its transmembrane domain. The CD40 ligand comprises residues 47-261, 1-23 or 47-261. The vector is rendered non-replicating in normal human cells. The method also comprises repeating the second step at a later time. The immune response includes the generation of cytotoxic CD8+ T cells against the antigen. The immune response includes the generation of antibodies against the antigen. The fusion protein is administered with an adjuvant. The fusion protein is administered subcutaneously. The sequence of CD40 ligand encoded by the vector and the sequence of CD40 ligand administered as a fusion protein are different. The sequence of the antigen encoded by the vector and the sequence of the antigen administered as a fusion protein are different. The transcription unit encodes a secretory signal sequence. The antigen is not from CD40 ligand. Treating an individual with cancer that expresses a tumor antigen comprises administering an expression vector comprising a transcription unit encoding a secretable fusion protein, comprising the tumor antigen and CD40 ligand and administering an effective amount of a fusion protein comprising the tumor antigen and CD40 ligand. The protein is administered after administration of the vector. The tumor antigen is a mucin antigen. The tumor antigen is the E7 protein of human papilloma virus. The cancer cells are epithelial or cervical cancer cells. The vector includes a human cytomegalovirus promoter/enhancer for controlling transcription of the transcription unit. The vector encodes a CD40L that includes no more than six residues from either end of the transmembrane domain. The vector does not encode the transmembrane domain of CD40 ligand. The CD40 ligand is missing all or substantially all of its transmembrane domain. The immune response includes the generation of antibodies against the tumor antigen. The fusion protein is administered with an adjuvant. The fusion protein is administered subcutaneously. Generating immunity in a subject to an infectious agent comprises administering an expression vector comprising a transcription unit encoding a secretable fusion protein, comprising an infectious agent antigen and CD40 ligand and administering an effective amount of a fusion protein comprising the infectious agent antigen and CD40 ligand. The protein is administered after administration of the vector. The infectious agent antigen is a viral antigen, bacterial antigen, fungal antigen or protozoan antigen. The infectious agent antigen is a viral antigen. The viral antigen is the E6 or E7 protein of human papilloma virus. The vector includes a human cytomegalovirus promoter/enhancer for controlling transcription of the transcription unit. The vector is a viral vector. The vector is an adenoviral vector. The CD40 ligand is human CD40 ligand. The CD40 ligand

lacks a cytoplasmic domain. The vector encodes a CD40L that includes no more than six residues from either end of the transmembrane domain. The vector does not encode the transmembrane domain of CD40 ligand. The CD40 ligand is missing all or substantially all of its transmembrane domain. The vector is rendered non-replicating in normal human cells. The fusion protein is administered with an adjuvant. The fusion protein is administered subcutaneously. The transcription unit encodes a secretory signal sequence. The antigen is not from CD40 ligand. Simultaneously producing an expression vector that encodes a fusion protein and the fusion protein comprises propagating in culture medium cells containing the expression vector, where the cells replicate the vector and produce the protein expressed from the vector into the culture medium during propagation.

ACTIVITY - Cytostatic; Virucide; Antibacterial; Fungicide; Protozoacide. No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The method is useful in generating an immune response (claimed) against a tumor, viral, bacterial, fungal or protozoan antigen.

ADMINISTRATION - The composition is administered via subcutaneous route (claimed). No dosage given.

EXAMPLE - No relevant examples given.(46 pages)

L4 ANSWER 6 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2005-21502 BIOTECHDS
TI New nucleic acid comprising Listeria monocytogenes hly 5' UTR or actA 5' UTR, a ribosome binding site (RBS) and a heterologous nucleic acid sequence, useful in inducing an immune response to a bacterial, fungal, parasitic or cancer antigen;
bacterium protein production and expression vector for use in vaccine and gene therapy
AU HIGGINS D E; SHEN A
PA HIGGINS D E; SHEN A
PI US 2005147621 7 Jul 2005
AI US 2004-961291 8 Oct 2004
PRAI US 2004-961291 8 Oct 2004; US 2003-510599 10 Oct 2003
DT Patent
LA English
OS WPI: 2005-487940 [49]
AN 2005-21502 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - An isolated nucleic acid (I) comprising a 5' untranslated region (UTR) from Listeria monocytogenes, a ribosome binding site, and a heterologous nucleic acid operably linked to the UTR, is new.

DETAILED DESCRIPTION - An isolated nucleic acid (I) comprises: (a) a 5' untranslated region (UTR) chosen from a Listeria monocytogenes hly 5' and actA 5' UTRs, and their functional fragments and variants; (b) a ribosome binding site (RBS); and (c) a heterologous nucleic acid sequence operably linked to the 5' UTR. INDEPENDENT CLAIMS are also included for: (1) an isolated nucleic acid comprising a L. monocytogenes 5' UTR chosen from an hly 5' UTR and an actA 5' UTR; (2) a nucleic acid vector comprising: (a) a Listeria monocytogenes promoter; (b) a Listeria monocytogenes hly or actA 5' UTR comprising a ribosome binding site; (c) a heterologous nucleic acid sequence; (d) a selectable marker; and (e) a bacterial origin of replication, where the UTR is operably linked to the promoter and the heterologous nucleic acid sequence; (3) a bacterium comprising a nucleic acid comprising the same components as the vector of (2); (4) a vaccine comprising the bacterium; (5) a vaccine comprising the isolated nucleic acid (I); (6) introducing an antigen into a eukaryotic cell comprising contacting the cell with the bacterium of (3); (7) inducing an immune response to an antigen in a subject by administering bacteria of (3); and (8) expressing a polypeptide by introducing nucleic acid (I) into a bacterium, where the

heterologous nucleic acid encodes a polypeptide, and expressing the polypeptide.

BIOTECHNOLOGY - Preferred Nucleic Acid: The nucleic acid (I) further comprises a promoter and preferably also a transcriptional activation site 5' of the promoter. The transcriptional activation site is a prfA box. The ribosome binding site (RBS) is the RBS that is naturally associated with the L. monocytogenes UTR. The hly 5' UTR comprises a nucleotide sequence at least 70% homologous to the sequence AGAGAGGGGTGGCAAACGGTATTTGGCATTATTAGGTTTGTAGAAGGAGAGTGAAACCC (SEQ ID NO. 3). The hyl 5' UTR comprises a nucleotide sequence at least 70% homologous to the sequence AGAAGCGAATTTCGCCAATATTATAATTATCAAAAGAGAGGGGTGG CAAACGGTATTTGGCATTATTAGGTTAAAAAATGTAGAAGGAGAGTGAAACCC (SEQ ID NO: 2). The hly 5' UTR comprises a nucleotide sequence at least 70% homologous to the sequence ATAAAGCAAGCATATAATATTGCGTTTCATCTTTAGAAGCGAATTTCGCCAATATTATAATTAT CAAAAGAGAGGGGTGGCAACGGTATTTGGCATTATTAGGTTAAAAAATGTAGAAGGAGAGTGAAACC (SEQ ID NO: 1). The actA 5' UTR comprises a nucleotide sequence at least 70% homologous to the sequence GTGAAAATGAAGGCCGAATTTTCCTTGTTCTAAAAAGGTTGTATTA GCGTATCACGAGGAGGGAGTATAA (SEQ ID NO. 7). The actA 5' UTR comprises a nucleotide sequence at least 70% homologous to the sequence GCTAATCCAATTTTTAACGGAATAAATTAGTGAAAATGAAGGCCGAATTTTCCTTGTTCTAAAAAGGTTGTAT TAGCGTATCACGAGGAGGGAGTATAA (SEQ ID NO. 6). The actA 5' UTR comprises a nucleotide sequence at least 70% homologous to the sequence TAATTCATGAATATTTTTTCTTATATTAGCTAATTAAGAAGATAATTAACTGCTAATCCAATTTTTAACGGAA TAAATTAGTGAAAATGAAGGCCGAATTTTCCTTGTTCTAAAAAGGTTGTATTAGCGTATCACGAGGAGGGAGT ATAA (SEQ ID NO: 5). The nucleic acid comprises an integration site. The heterologous nucleic acid encodes a viral polypeptide or its antigenic fragment. The heterologous nucleic acid encodes an inhibitory RNA or its portion. The viral polypeptide is a viral polypeptide encoded by human immunodeficiency virus, hepatitis B virus, hepatitis C virus, hepatitis A virus, smallpox, influenza viruses, human papilloma viruses, adenoviruses, rhinoviruses, coronaviruses, herpes simplex virus, respiratory syncytial viruses, rabies or coxsackie virus. The viral polypeptide comprises influenza antigens such as hemagglutinin (HA), nucleoprotein (NP), matrix protein (MP1); HIV antigens such as HIV gag, pol, env, tat, reverse transcriptase hepatitis; viral antigens such as the S. M, and L proteins of hepatitis B virus, the pre-S antigen of hepatitis B virus, and other hepatitis, e.g., hepatitis A, B, and C, viral components such rubella virus components; rotaviral antigens such as VP7sc and other rotaviral components; cytomegaloviral antigens such as envelope glycoprotein B and other cytomegaloviral antigen components; respiratory syncytial viral antigens such as the RSV fusion protein, the M2 protein and other respiratory syncytial viral antigen components; herpes simplex viral antigens such as immediate early proteins, glycoprotein D, and other herpes simplex viral antigen components; varicella zoster viral antigens such as gpI, gpII, and other varicella zoster viral antigen components; Japanese encephalitis viral antigens such as proteins E, M-E, M-E-NS 1, NS 1, NS 1-NS2A, and other Japanese encephalitis viral antigen components; rabies viral antigens such as rabies glycoprotein, rabies nucleoprotein and other rabies viral antigen components; and Hepatitis B surface antigen; hepatitis C viral RNA; influenza viral antigens such as hemagglutinin and neuraminidase and other influenza viral components; measles viral antigens such as the measles virus fusion protein and other measles virus components; rubella viral antigens such as proteins E1 and E2. The heterologous nucleic acid sequence encodes a mammalian polypeptide. The mammalian polypeptide is a cancer-associated polypeptide or its antigenic fragment. The nucleic acid cancer-associated polypeptide comprises 707 alanine proline (707-AP); alpha ((x)-fetoprotein (AFP); adenocarcinoma antigen recognized by T cells 4 (ART-4); B antigen (BAGE); beta-catenin/mutated(b-catenin/m); breakpoint cluster region-Abelson (Bcr-abl); CTL-recognized antigen on melanoma (CAMEL); carcinoembryonic antigen peptide-1 (CAP-1); caspase-8 (CASP-8); cell-division cycle 27 mutated (CDC27m); cyclin-dependent kinase 4 mutated CDK4/m); carcinoembryonic antigen (CEA); cancer/testis (CT) antigen; cyclophilin B

(Cyp-B); differentiation antigen melanoma (DAM-6, also known as MAGEB2, and DAM-10, also known as MAGE-B1); elongation factor 2 mutated (ELF2M); Ets variant gene 6/acute myeloid leukemia i gene ETS (ETV6-AML1); glycoprotein 250 (G250); G antigen (GAGE); N-acetylglucosaminyltransferase V (GnT-V); glycoprotein 100 kD (GnT-V); helicase antigen (HAGE); human epidermal receptor-2/neurological (HER-2/neu); HLA-Aasterisk0201-R1701 (HLA-Aasterisk0201 having an arginine (R) to isoleucine (I) exchange at residue 170 of the (x-helix of the (x2-domain in the HLA-A2 gene); human papilloma virus E7 (HPV-E7); human papilloma virus E6 (HPV-E6); heat shock protein 70-2 mutated (HSP70-2M); human signet ring tumor-2 (HST-2); human telomerase reverse transcriptase (hTERT or hTRT); intestinal carboxyl esterase (iCE); KIAA0205; L antigen (LAGE); low density lipid receptor/GDP-L-fucose: beta-D-galactosidase 2-(alpha-Lfucosyltransferase (LDLR/FUT); melanoma antigen (MAGE); melanoma antigen recognized by T cells-1/Melanoma antigen A (MART-1/Melan-A); melanocortin i receptor (MCiR); myosin mutated (myosin/m); mucin 1 (MUC 1); melanoma ubiquitous mutated 1 (MUM-1), melanoma ubiquitous mutated 2 (MUM-2), melanoma ubiquitous mutated 3 (MUM-3); New York-esophageous 1 (NY-ESO-1); protein 15 (P15); protein of 190 KD bcr-abl (pl90 minor bcr-abl); promyelocytic leukemia/retinoic acid receptor alpha (Pml/ RARa); preferentially expressed antigen of melanoma (PRAME); prostate-specific antigen (PSA); prostate-specific membrane antigen (PSM); renal antigen (RAGE); renal ubiquitous i (RU1), renal ubiquitous 2 (RU2); sarcoma antigen (SAGE); SART-1; SART-3; translocation Ets-family leukemia/acute myeloid leukemia 1 (TEL/AML1); triosephosphate isomerase mutated (TPI/m); tyrosinase related protein i (TRP-1 or gp75); tyrosinase related protein 2 (TRP2); TRP-2/intron 2 (TRP-2/INT2); Wilms' tumor gene (WT-1). The heterologous nucleic acid sequence encodes a bacterial polypeptide or its antigenic fragment. The nucleic acid bacterial polypeptide is a bacterial polypeptide encoded by one of the following bacteria: Mycobacterium spp. (e.g., Mycobacterium tuberculosis, Mycobacterium leprae), Streptococcus spp. (e.g., Streptococcus pneumoniae, Streptococcus pyogenes), Staphylococcus spp. (e.g., Staphylococcus aureus), Treponema (e.g., Treponema pallidum), Chlamydia spp., Vibrio spp. (e.g., Vibrio cholerae), Bacillus spp. (e.g., Bacillus subtilis Bacillus anthracis), Yersinia spp. (e.g., Yersinia pestis), Neisseria spp. (e.g., Neisseria meningitides, Neisseria gonorrhoeae), Legionella spp., Bordetella spp. (e.g., Bordetella pertussis), Shigella spp., Campylobacter spp., Pseudomonas spp. (e.g., Pseudomonas aeruginosa), Brucella spp., Clostridium spp. (e.g., Clostridium tetani, Clostridium botulinum, Clostridium perfringens), Salmonella spp. (e.g., Salmonella typhi), Borrelia spp. (e.g., Borrelia burgdorferi), Rickettsia spp. (e.g., Rickettsia prowazeki), Mycoplasma spp. (e.g., Mycoplasma pneumoniae), Haemophilus spp. (e.g., Haemophilus influenzae), Branhamella spp. (e.g., Branhamella catarrhalis), Corynebacteria spp. (e.g., Corynebacteria diphtheriae), Klebsiella spp. (e.g., Klebsiella pneumoniae), Escherichia spp. (e.g., Escherichia coli), and Listeria spp. (e.g., Listeria monocytogenes). The bacterial polypeptide comprises listeriolysin O, L. monocytogenes p60, L. monocytogenes metalloprotease (MPL), Chlamydia Capl, Chlamydia Cap2, M. tuberculosis heat shock protein (hsp)60, M. tuberculosis hsp70, M. tuberculosis Ag85, M. tuberculosis' ESAT-6 and M. tuberculosis' CFP10. The heterologous nucleic acid sequence encodes a parasitic or fungal polypeptide. The parasitic or fungal polypeptide is a polypeptide encoded by one of the following parasites or fungi: Candida spp. (e.g., Candida albicans), Cryptococcus spp. (e.g., Cryptococcus neoformans), Aspergillus spp., Histoplasma spp. (e.g., Histoplasma capsulatum), Coccidioides spp. (e.g., Coccidioides immitis), Pneumocystis (e.g., Pneumocystis cariniO, Entamoeba spp. (e.g., Entamoeba histolytica), Giardia spp., Leishmania spp., Plasmodium spp., Trypanosoma spp., Toxoplasma spp. (e.g., Toxoplasma gondii), Cryptosporidium spp., Trichuris spp. (e.g., Trichuris trichiura), Trichinella spp. (e.g., Trichinella spiralis), Enterobius spp. (e.g., Enterobius vermicularis), Ascaris spp. (e.g., Ascaris lumbricoides), Ancylostoma spp., Strongyloides spp., Filaria spp., and

Schistosoma spp. The parasitic polypeptide is MSP-1; malarial antigens 41-3, AMA-1, CSP, PFEMP-1, GBP-130, MSP-1, PFS-16, SERP; fungal antigens such as heat shock protein 60; plasmodium falciparum antigens such as merozoite surface antigens, sporozoite surface antigens, circumsporozoite antigens, gametocyte/gamete surface antigens, blood-stage antigen pf i 55/RESA and other plasmodial antigen components; toxoplasma antigens such as SAG-1, p30 and other toxoplasma antigen components; schistosomae antigens such as glutathione-S-transferase, paramyosin, and other schistosomal antigen components; leishmania major and other leishmaniae antigens such as gp63, lipophosphoglycan and its associated protein and other leishmanial antigen components; and Trypanosoma cruzi antigens such as the 75-77 kDa antigen, the 56 kDa antigen and other trypanosomal antigen components. The Listeria monocytogenes 5' UTR increases expression of a polypeptide encoded by the heterologous nucleic acid sequence at least 1.5-fold, 2-fold, 5-fold, 10-fold, 30-fold, or 50-fold relative to a polypeptide encoded by the heterologous nucleic acid sequence that is not operably linked to the UTR. Preferred Bacterium: The bacterium is a Listeria monocytogenes bacterium, a Bacillus subtilis bacterium or a Lactococcus lactis bacterium.

ACTIVITY - Antiviral; Antibacterial; Fungicide; Antiparasitic; Cytostatic. No biological data given.

MECHANISM OF ACTION - Vaccine; Gene therapy.

USE - The nucleic acid and the bacterium containing the nucleic acid are useful as antiviral, antibacterial, antifungal, antiparasitic and cancer vaccines. The nucleic acid is useful for expressing an inhibitory RNA. A bacterium transfected by the nucleic acid is useful for production of a polypeptide. (All claimed).

ADVANTAGE - The hly and actA 5' UTRs give enhanced expression of heterologous nucleic acids. Bacteria (e.g. Listeria monocytogenes, Bacillus subtilis or Lactococcus lactis) transfected with a nucleic acid including one of the 5' UTRs may be used for expression of a heterologous polypeptide, especially where expression in a bacterium such as Escherichia coli is not appropriate, e.g. where the polypeptide is toxic to E. coli.(26 pages)

L4 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
AN 2005:577956 CAPLUS
DN 143:113718
TI A Single Vaccination with Polyomavirus VP1/VP2Her2 Virus-Like Particles Prevents Outgrowth of HER-2/neu-Expressing Tumors
AU Tegerstedt, Karin; Lindencrona, Jan Alvar; Curcio, Claudia; Andreasson, Kalle; Tullus, Carl; Forni, Guido; Dalianis, Tina; Kiessling, Rolf; Ramqvist, Torbjoern
CS Department of Oncology-Pathology, Karolinska Institutet, Cancer Centrum Karolinska, Stockholm, Swed.
SO Cancer Research (2005), 65(13), 5953-5957
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB Murine polyomavirus (MPyV) VP1 virus-like particles (VLPs), containing a fusion protein between MPyV VP2 and the extracellular and transmembrane domain of HER-2/neu (Her2), Her21-683PyVLPs, were tested for their ability to vaccinate against Her2-expressing tumors in two different in vivo models. Protection was assessed both against a lethal challenge with a BALB/c mammary carcinoma transfected with human Her2 (D2F2/E2) and against the outgrowth of autochthonous mammary carcinomas in BALB-neuT mice, transgenic for the activated rat Her2 oncogene. A single injection of Her21-683PyVLPs before tumor inoculation induced a complete rejection of D2F2/E2 tumor cells in BALB/c mice. Similarly, a single injection of Her21-683PyVLPs at 6 wk of age protected BALB-neuT mice with atypical hyperplasia from a later outgrowth of mammary carcinomas, whereas all controls developed palpable tumors in all mammary glands. VLPs containing only VP1 and VP2 did not induce

protection. The protection elicited by Her21-683PyVLPs vaccination was most likely due to a cellular immune response because a Her2-specific response was shown in an ELISPOT assay, whereas antibodies against Her2 were not detected in any of the two models. The results show the feasibility of using MPyV-VLPs carrying Her2 fusion proteins as safe and efficient vaccines against Her2-expressing tumors.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-25807 BIOTECHDS
TI New pestivirus replicon, comprising a pestivirus nucleic acid sequence and a heterologous antigen-encoding sequence, useful for inducing a T cell response to an antigen in a subject;
involving vector-mediated gene transfer and expression in host cell for therapy
AU REHERMANN B; RACANELLI V; BEHRENS S; TAUTZ N
PA UNIV GIESSEN JUSTUS-LIEBIG; US DEPT HEALTH and HUMAN SERVICES
PI WO 2004092386 28 Oct 2004
AI WO 2004-US11018 10 Apr 2004
PRAI US 2003-463097 14 Apr 2003; US 2003-462165 11 Apr 2003
DT Patent
LA English
OS WPI: 2004-758347 [74]
AN 2004-25807 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - A pestivirus replicon, comprising a pestivirus nucleic acid sequence and a heterologous antigen-encoding sequence, where the antigen-encoding sequence is inserted at a position in the pestivirus nucleic acid sequence that inhibits formation of infectious replicon particles by disrupting the expression of structural proteins required for formation of infectious replicons, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) inducing a T cell response to an antigen in a subject, comprising administering to a subject an amount of an antigen presenting cell sufficient to induce a T cell response in the subject, where the antigen presenting cell expresses an antigen from the pestivirus replicon, thus inducing a T cell response to the antigen in the subject; (2) an isolated nucleic acid molecule, where the nucleic acid molecule comprises a sequence of, or having at least 90% sequence identity to a sequence of 10794 or 12042 bp (S1-S2), fully defined in the specification; (3) a transfected dendritic cell into which a pestivirus replicon that expresses an antigen , or the pestivirus replicon cited above has been introduced ex vivo; (4) compositions for inducing an immune response, where the composition comprises a sequence of, or having at least 90% identity to 2386 or 2802 amino acids, fully defined in the specification, or its conservative variant, or the nucleic acid molecule that encodes such proteins; and (5) a pharmaceutical composition comprising the components of the composition cited above, and a carrier.

BIOTECHNOLOGY - Preferred Replicon: The pestivirus replicon comprises a bovine viral diarrhea virus (BVDV), classical swine fever virus (CSFV) or border disease virus (BDV). The pestivirus is preferably BVDV. The antigen-encoding sequence disrupts the expression of at least one of the C, Ems, E1, or E2 subunits of the pestivirus nucleic acid sequence. The antigen-encoding sequence partially or completely replaces the C, Ems, E1, or E2 subunits of the pestivirus nucleic acid sequence. The replicon is monocistronic or bicistronic. One open reading frame of the bicistronic replicon comprises an Npro-encoding sequence and the heterologous antigen-encoding sequence. The replicon comprises an RNA sequence that encodes an Npro-antigen fusion protein and a polyprotein comprising NS2/NS3, NS4A, NS4B, NS5A, and NS5B, where NS2/N3 comprises uncleaved NS2-NS3 polypeptide or NS3 polypeptide. The

NS2/N3 is uncleaved NS2-NS3 polypeptide. The NS2/N3 is NS3 polypeptide. The RNA sequence comprises the following elements: 5'-IRES-Npro-Antigen-IRES-p7-(NS2-NS3)-NS4A-NS4B-NS5A-NS5B-3', where Antigen is the heterologous antigen-encoding sequence. The RNA sequence is encoded by a nucleic acid sequence comprising S1 or S2. The antigen-encoding sequence encodes an antigen of a pathogen or tumor. The antigen comprises one or more epitopes. The antigen is an antigen of a pathogen. The pathogen is a viral pathogen. The viral pathogen is a Hepatitis C virus, a Human Immunodeficiency Virus, or a Respiratory Syncytial Virus. The antigen is HCV core, HCV E1, HCV E2, HCV p7, HCV NS2, HCV NS3, HCV NS4, or HCV NS5. The replicon comprises an antigen comprising a sequence of, or that is at least 90, 95 or 98% identical to 798 amino acids, fully defined in the specification. The viral pathogen is a Respiratory Syncytial Virus and the antigen is RSV F, RSV N3 RSV M2 or RSV G. The viral pathogen is a Human Immunodeficiency Virus and the antigen is p18, p24, p33, p39, p55, gp36, gp41, gp120. The pathogen is a bacterial pathogen, preferably Mycobacterium tuberculosis or Plasmodium falciparum. The antigen is ESAT-6, MPT63, MPT64, MPT83, Antigen 85B, Antigen 85A, PstS-1, PstS-2 or PstS-3, MTB41, or hsp60. The antigen is circumsporozoite protein (CSP), thrombospondin-related adhesive protein (TRAP), sporozoite and liver-stage antigen (SALSA), sporozoite threonine- and asparagine-rich protein (STARP), merozoite surface protein (MSP)-1, -2, 3, -4, -5, erythrocyte-binding antigen (EBA)-175, apical membrane antigen (AMA)-1, rhoptry-associated protein (RAP)-I and-2, acidic-basic repeat antigen (ABRA)5 ring erythrocyte surface antigen (RESA), serine-rich protein (SERF), erythrocyte membrane protein (EMP)-I1 -2 and -3, Glutamate-rich protein (GLURP), Glycosilphosphatidylinositol (GPI), Ps25, Ps28, Ps48/45 or Ps230. The antigen is a tumor antigen, preferably Her-2/neu, alpha-fetoprotein, human epithelial cell mucin, the Ha-ras oncogene product, p53, carcino-embryonic antigen, the raf oncogene product, GD2, GD3, GM2, TF, sTn, MAGE-1, MAGE-3, tyrosinase, gp75, Melan-AlMart-1, gpIOO, EBV-LNT 1, EBV-LNT 2, HPV-F4, HPV-F 6, HPV-F 7, prostatic serum antigen, CO 17-1A, GA733, gp72, p53, the ras oncogene product, BPV E7 or melanoma ganglioside.Preferred Method: Inducing a T cell response to an antigen in a subject further comprises transfecting the antigen-presenting cell with the pestivirus replicon prior to administering the antigen-presenting cell to the subject. The antigen-presenting cell is a dendritic cell or a fibroblast. The antigen-presenting cell is an autologous cell. The replicon is a cytopathic or non-cytopathic replicon. The antigen is an antigen of a pathogen or tumor as cited above.

USE - The replicons are useful for inducing a T cell response (claimed), and for generating a T cell-mediated immunity, particularly T cell-mediated immunity to Hepatitis C virus (HCV), respiratory syncytial virus (RSV), human immunodeficiency virus (HIV), Mycobacterium tuberculosis, Plasmodium falciparum and tumors. (143 pages)

L4 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:118581 CAPLUS
DN 138:168816
TI Engineered transmembrane proteins: spontaneous insertion and antitumor activity of TSST-1 fusion proteins
IN Wahlsten, Jennifer L.; Ramakrishnan, Sundaram; Schlievert, Patrick M.
PA USA
SO U.S. Pat. Appl. Publ., 37 pp., Division of U.S. Ser. No. 1,593, abandoned.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003032582	A1	20030213	US 1999-465714	19991217
PRAI US 1997-1593	B3	19971231		

AB The authors disclose membrane-infiltrating polypeptides that have the

ability to insert spontaneously into cell membranes. These membrane-infiltrating polypeptides generally include a membrane-infiltrating amino acid sequence as well as another amino acid sequence heterologous to the membrane-infiltrating sequence. In one example, the authors prepare constructs of staphylococcal toxic shock syndrome toxin (TSST-1) fused N-terminal to the transmembrane domain of c-erb-B2. The constructs exhibit spontaneous insertion into the plasma membranes of tumor cell lines; the treated cells stimulate T-cell proliferation and an antitumor immune response. In addition, an N-terminal fragment of TSST-1 is shown to bind MHC class II mols. and inhibit the toxic effects associated with the non-truncated toxin.

L4 ANSWER 10 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-05183 BIOTECHDS
TI New fusion partner protein, useful in medicine, or in manufacturing an immunogenic composition for eliciting an immune response in a patient or treating a patient suffering from or susceptible to cancer or infectious diseases;
recombinant protein production via plasmid expression in host cell for use in vaccine
AU CABEZON SILIVA T E V; ELLIS J H; GERARD C M G; HAMBLIN P A; PALMANTIER R M; VINALS Y DE BASSOLS C
PA GLAXOSMITHKLINE BIOLOGICALS SA; GLAXO GROUP LTD
PI WO 2003104272 18 Dec 2003
AI WO 2003-EP6096 6 Jun 2003
PRAI GB 2003-914 15 Jan 2003; GB 2002-13365 11 Jun 2002
DT Patent
LA English
AN 2004-05183 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - A fusion partner protein comprising a choline binding domain and a heterologous promiscuous T helper epitope, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a nucleic acid sequence encoding the protein; (2) an expression vector comprising the nucleic acid sequence; (3) a host transformed with the nucleic acid sequence or the expression vector; (4) an immunogenic composition comprising the protein or the nucleic acid sequence and a pharmaceutical carrier; (5) preparing the immunogenic composition comprising admixing the protein or the nucleic acid sequence with an adjuvant, diluent or other pharmaceutical carrier; (6) producing the fusion protein comprising culturing the host cell under conditions sufficient for the production of the fusion protein, and recovering the fusion protein from the culture medium; and (7) treating a patient suffering from cancer by administering the immunogenic composition.
BIOTECHNOLOGY - Preferred Fusion Protein: The choline binding domain is derived from the C terminus of LytA. The C-LytA or derivatives comprise at least four repeats of any one of 6 sequences of 15-23 amino acids (I), fully defined in the specification. The choline binding domain comprises: (a) the C-terminal domain of LytA having a sequence of 142 amino acids (II), fully defined in the specification; (b) a sequence of 112 amino acids (III), fully defined in the specification; (c) a peptide sequence comprising an amino acid sequence having at least 85%, 90%, 95%, or 97-99% identity to any one of the sequences of (I); or (d) a peptide sequence comprising an amino acid sequence having at least 15, 20, 30, 40, 50 or 100 contiguous amino acids from the amino acid sequence of (II) or (III). The fusion partner protein further comprises a heterologous protein, which is chemically conjugated to the fusion partner. The heterologous protein is derived from an organism, such as human immunodeficiency virus HIV-1, human herpes simplex viruses, cytomegalovirus, rotavirus, Epstein-Barr virus, varicella-zoster virus, hepatitis virus, e.g. hepatitis B virus, hepatitis A virus, hepatitis C virus or hepatitis E virus, respiratory syncytial virus, parainfluenza virus, measles virus, mumps virus, human papilloma viruses, flaviviruses,

influenza virus, Neisseria spp., Moraxella spp., Bordetella spp., Mycobacterium spp., including Mycobacterium tuberculosis, Escherichia coli, including enterotoxic Escherichia coli, Salmonella spp., Listeria spp., Helicobacter spp., Staphylococcus spp., including Staphylococcus aureus, Staphylococcus epidermidis, Borrelia spp., Chlamydia spp., including Chlamydia trachomatis, Chlamydia pneumoniae, Plasmodium spp., including Plasmodium falciparum, Toxoplasma spp., or Candida spp.. The heterologous protein is a tumor associated protein or tissue specific protein, or its immunogenic fragment. The heterologous protein or its fragment is MAGE 1, MAGE 3, MAGE 4, PRAME, BAGE, LAGE 1, LAGE 2, SAGE, HAGE, XAGE, PSA, PAP, PSCA, prostein, P501S, HASH2, Cripto, B726, NY-BR1.1, P510, MUC-1, prostase, STEAP, tyrosinase, telomerase, survivin, CASB616, P53, or Her-2/neu. The fusion protein further comprises an affinity tag of at least 4 histidine residues. Preferred Immunogenic Composition: The immunogenic composition additionally comprises a T helper-1 inducing adjuvant, e.g. 3D-MPL, QS21, a mixture of QS21 and cholesterol, a CpG oligonucleotide, or a mixture of two or more of the adjuvants. The DNA sequence is coated onto biodegradable beads or delivered via a particle bombardment approach. The protein is adjuvanted.

ACTIVITY - Cytostatic; Antimicrobial.

MECHANISM OF ACTION - Vaccine. Groups of 5-10, eight-week old female C57BL6 mice were vaccinated, 2-6 times intramuscularly at 2 weeks intervals with 10 microg of the CPC-P501S protein formulated in different adjuvant systems. The serology (total immunoglobulin response) and cellular response (T cell lymphoproliferation and cytokine production) were analyzed on spleen cells, 6-14 days after the last vaccination. The adjuvanted CPC-P501S proteins gave a good antibody response after vaccination. A P501 specific lymphoproliferation was seen in the spleen of all groups of mice receiving the adjuvanted protein after in vitro re-stimulation with the immunogen or another P501 protein made in another expression system indicating that T cells have been primed in vivo by vaccination.

USE - The fusion partner protein or nucleic acid sequence is useful in medicine, or in manufacturing an immunogenic composition for eliciting an immune response in a patient by sequential administration of the protein followed by the DNA sequence, or the DNA sequence followed by the protein, or for treating a patient suffering from or susceptible to cancer, e.g. prostate cancer, colorectal cancer, lung cancer, breast cancer or melanoma (all claimed). The immunogenic composition is also useful for treating infectious diseases.

ADMINISTRATION - Administration of the composition is intramuscularly, subcutaneously, intraperitoneally, or intravenously. No dosage details given.

EXAMPLE - The P2 sequence of tetanus toxin was inserted in frame, inside the C-lytA coding sequence. The C-lytA coding sequence was harbored by plasmid pRIT 14662. After ligation and transformation of Escherichia coli and transformant characterization, the plasmid named pRIT15199 was obtained. PCR amplification was performed using the plasmid as template and the oligonucleotides C-lytANOTATG and C-lytA-aa55. The amplified fragment was treated with the restriction enzymes NcoI abd Afl III to generate the cohesive ends. The fragment was ligated with vector pRIT15068 to generate the complete fusion protein coding sequence. The plasmid pRIT15200 was obtained after ligation and E. coli transformation. The NcoI fragment isolated from pRIT 15202 was ligated to pRIT 15200 generating the final expression plasmid pRIT15201, which was used to transform the Saccharomyces cerevisiae strain DC5. After selection and characterization of the yeast transformants containing the plasmid pRIT 15201, a recombinant yeast strain named Y1796 expressing CPC-P501-His fusion protein was obtained. The protein after reduction and carboxyamidation, was isolated and purified by affinity chromatography followed by anion exchange chromatography. (162 pages)

L4 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4
AN 2003:273815 CAPLUS
DN 138:400053
TI A Chimeric Multi-Human Epidermal Growth Factor Receptor-2 B Cell Epitope Peptide Vaccine Mediates Superior Antitumor Responses
AU Dakappagari, Naveen K.; Pyles, John; Parihar, Robin; Carson, William E.; Young, Donn C.; Kaumaya, Pravin T. P.
CS Departments of Obstetrics and Gynecology, Ohio State University, Columbus, OH, 43210, USA
SO Journal of Immunology (2003), 170(8), 4242-4253
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB Immunotherapeutic approaches to cancer should focus on novel undertakings that modulate immune responses by synergistic enhancement of antitumor immunol. parameters. Cancer vaccines should preferably be composed of multiple defined tumor Ag-specific B and T cell epitopes. To develop a multiepitope vaccine, 12 high ranking B cell epitopes were identified from the extracellular domain of the human epidermal growth factor receptor-2 (HER-2) oncoprotein by computer-aided anal. Four novel HER-2 B cell epitopes were synthesized as chimeras with a promiscuous T cell epitope (aa 288-302) from the measles virus fusion protein (MVF). Two chimeric peptide vaccines, MVF HER-2316-339 and MVF HER-2485-503 induced high levels of Abs in outbred rabbits, which inhibited tumor cell growth. In addition, Abs induced by a combination of two vaccines, MVF HER-2316-339 and MVF HER-2628-647 down-modulated receptor expression and activated IFN-γ release better than the individual vaccines. Furthermore, this multiepitope vaccine in combination with IL-12 caused a significant reduction ($p = 0.004$) in the number of pulmonary metastases induced by challenge with syngeneic tumor cells overexpressing HER-2. Peptide Abs targeting specific sites in the extracellular domain may be used for exploring the oncoprotein's functions. The multiepitope vaccine may have potential application in the treatment of HER-2-associated cancers.
RE.CNT 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5
AN 2003:886459 CAPLUS
DN 140:197974
TI Anti-Her-2/neu-IL-2 or heregulin-IL-2 fusions proteins redirect non-tumor specific CTL to the tumor site for tumor eradication
AU Lustgarten, Joseph
CS Sidney Kimmel Cancer Center, San Diego, CA, 92121, USA
SO Cancer Immunology Immunotherapy (2003), 52(12), 751-760
CODEN: CIIMDN; ISSN: 0340-7004
PB Springer-Verlag
DT Journal
LA English
AB Interleukin 2 (IL-2) is a T-cell growth factor that has pleiotropic functions on T cells, assisting in activating and expanding immune responses. The authors have previously found that in the presence of IL-2, CD4+ or CD8+ T cells kill tumor cells in an antigen-independent and non-MHC-restricted manner. Here, they took advantage of IL-2 capabilities to induce in this way the killing of tumor cells for immunotherapeutic purposes. They describe a novel mechanism where it is possible to bypass the usage of tumor-specific T cells for adoptive transfer by using non-tumor-specific T cells in combination with an anti-Her-2/neu-IL-2 (neu-Ab-IL-2) or heregulin-IL-2 fusion protein for tumor eradication. T cells in the presence of fusion proteins are capable of inducing

the lysis of tumor cells in a non-MHC-restricted manner. This lysis is only observed in T cells that have been stimulated through the TCR, and is mediated via the Fas-FasL pathway. Moreover, transfer of non-tumor-specific T cells in combination with the fusion proteins, induced the eradication of established Her-2, Her-3, and Her-4 expressing tumor cells in SCID mice. In contrast, the combination of non-tumor-specific T cells plus rIL-2 or irrelevant Ab-IL-2 (anti-hemagglutinin-IL-2) does not induce the elimination of tumors, indicating that the antitumor activity is dictated by the specificity of the fusion protein. Thus, neu-Ab-IL-2 or heregulin-IL-2 fusion proteins can direct the non-tumor-specific T cells to the tumor site and induce the elimination of tumors. The combination of non-tumor-specific T cells and antibody/ligand-IL-2 fusion proteins therefore provides an alternative therapeutic strategy to control tumor growth in vivo.

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:974170 CAPLUS
DN 139:148011
TI Oncogenes as targets for cancer vaccines
AU Khleif, Samir N.; Lucci, Joseph A., III
CS Cancer Vaccine Clinic, NCI-Naval Hospital Bethesda, National Cancer Institute, Bethesda, MD, USA
SO Oncogene-Directed Therapies (2003), 433-452. Editor(s): Rak, Janusz. Publisher: Humana Press Inc., Totowa, N. J.
CODEN: 69DKTX; ISBN: 0-89603-982-X
DT Conference; General Review
LA English
AB A review. It has been long known that the immune system interacts with tumor cells and scientists have long believed that tumors carry surface mols., antigens, that are recognized by the immune system and can induce a protective immune response. Advances in mol. biol. and immunol. in the past two decades have provided concrete evidence for the presence of these antigens, which are called tumor-associated antigens (TAA) and also provided the tools for the potential development of immunol. approaches to target cells carrying these antigens. The concept of immunotherapy for cancer is over 100 yr old. The first reported cancer vaccine trial was by W. B. Coley in 1894. Coley's toxin, as it was called, was not so much a vaccine as a nonspecific immunostimulant. He used 13 different prepns. of bacterial exts., between 1892 and 1936, to treat patients with a variety of malignancies with surprising success. He and others, including investigators at Mayo Clinic, reported over 50 % durable responses in patient populations where 10-15 % survival was historically expected. About the same time, in the early 1900s, Paul Ehrlich proposed the concept of immune surveillance. Ehrlich suggested that tumors present unique antigens that could be recognized by the immune system, leading to continuous identification and removal of transformed cells. It was another 50 yr before his theory could be proven. In the 1950s, when inbred mouse strains became available, Ehrlich's theory was tested and proved the immunogenicity of tumors. The tumor antigens were subsequently identified. The field of immunol. has provided the knowledge of how internal and external proteins are processed by the cell and presented to the immune system as TAA as a requirement for antigen recognition, immune activation, and immune response. This review seeks to provide a basic understanding of these concepts and how they are applied to current tumor vaccine development. Also, we will discuss how oncogenes products serve as TAA and form some of the most ideal targets for the development of targeted vaccine therapy against cancer.

RE.CNT 153 THERE ARE 153 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6
AN 2002:123077 CAPLUS
DN 136:178974
TI Construction and purification of Her-2/neu fusion proteins and their use to inhibit cancer cell growth
IN Cheever, Martin A.; Gheysen, Dirk
PA Corixa Corporation, USA; Smithkline Beecham Biologicals SA
SO PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002012341	A2	20020214	WO 2001-US24283	20010803
	WO 2002012341	A3	20030417		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2417915	AA	20020214	CA 2001-2417915	20010803
	AU 2001079153	A5	20020218	AU 2001-79153	20010803
	EP 1328631	A2	20030723	EP 2001-957404	20010803
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004521609	T2	20040722	JP 2002-518312	20010803
PRAI	US 2000-632507	A	20000803		
	WO 2001-US24283	W	20010803		

AB The present invention is generally directed to Her-2/neu fusion proteins, nucleic acid mols. encoding Her-2/neu fusion proteins, viral vectors expressing Her-2/neu fusion proteins, and pharmaceutical compns. (e.g., vaccines) comprising the Her-2/neu fusion proteins and/or nucleic acid mols. encoding the Her-2/neu fusion proteins. Thus, fusion proteins are constructed comprising the N-terminal extracellular domain of human, rat, or murine Her-2/neu fused to either the phosphorylation domain or the intracellular domain of Her-2/neu. In some constructs, a six-amino acid fragment of ribosomal P protein is fused to the C-terminus of the fusion construct. The fusion proteins are expressed in better yield than full-length Her-2/neu while retaining activity to inhibit cancer cell growth. Expression vectors are described for production of Her-2/neu fusion constructs in CHO cells, BHK cells, HEK-293 cells, Escherichia coli, and Pichia. The expressed proteins are purified by a two-step procedure: anion-exchange on Q Sepharose followed by hydrophobic chromatograph on Phenyl-Sepharose 6 Fast Flow. Thus, the present invention is also directed to methods of treating or preventing cancer by eliciting or enhancing an immune response to the Her-2/neu fusion proteins, including for uses in the treatment of malignancies associated with the Her-2/neu oncogene.

L4 ANSWER 15 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2003-05372 BIOTECHDS

TI New nucleic acid molecule encoding an antigenic fusion polypeptide useful as vaccines for enhancing or inducing immune responses , primarily cytotoxic T lymphocytes (CTL) responses to specific antigens such as tumor or viral antigens;
vector-mediated recombinant protein gene transfer and expression in host cell for use in cancer and HIV virus infection therapy and recombinant vaccine preparation

AU WU T; HUNG C
PA UNIV JOHNS HOPKINS

PI WO 2002074920 26 Sep 2002
AI WO 2002-US8033 18 Mar 2002
PRAI US 2001-276854 16 Mar 2001; US 2001-276854 16 Mar 2001
DT Patent
LA English
OS WPI: 2002-740856 [80]
AN 2003-05372 BIOTECHDS

AB DERWENT ABSTRACT:
NOVELTY - A nucleic acid molecule that encodes a fusion polypeptide, comprising a first nucleic acid sequence encoding a polypeptide that comprises at least one immunogenicity-potentiating polypeptide, optionally, fused in frame with the nucleic acid, a linker nucleic acid encoding a linker peptide, and a nucleic acid that is linked in frame to them, and that encodes an antigenic peptide or polypeptide, is new.

DETAILED DESCRIPTION - A nucleic acid molecule that encodes a fusion polypeptide, comprising a first nucleic acid sequence encoding a polypeptide that comprises at least one immunogenicity-potentiating polypeptide, optionally, fused in frame with the nucleic acid, a linker nucleic acid encoding a linker peptide, and a nucleic acid that is linked in frame to them, and that encodes an antigenic peptide or polypeptide, is new. The nucleic acid molecule is in the form of a replicon-defective alphavirus replicon particle prepared using a packaging cell line. INDEPENDENT CLAIMS are also included for the following: (1) an expression vector comprising the nucleic acid molecule operatively linked to a promoter, and optionally, additional regulatory sequences that regulate expression of the nucleic acid in a eukaryotic cell; (2) a cell, which has been modified to comprise the nucleic acid or the expression vector; (3) a pharmaceutical composition capable of inducing or enhancing an antigen-specific immune response, comprising an excipient and the nucleic acid molecule, expression vector and/or the cell; (4) inducing or enhancing an antigen specific immune response in cells or a subject; (5) increasing the numbers or lytic activity of the CD8+ cytotoxic T lymphocytes (CTL) specific for a selected antigen in a subject; and (6) inhibiting growth or preventing re-growth of a tumor in a subject.

BIOTECHNOLOGY - Preferred Nucleic Acid: The first polypeptide of the nucleic acid molecule is the one that acts by promoting: (a) processing of the linked antigenic polypeptide through the major histocompatibility complex (MHC) class I pathway or targeting of a cellular compartment that increases the processing; (b) development, accumulation or activity of antigen presenting cells or targeting of antigen to compartments of the antigen presenting cells leading to enhanced antigen presentation; (c) intercellular transport and spreading of the antigen; or (d) any combination of (a)-(c). The first polypeptide is: (a) a mycobacterial HSP70 polypeptide, its C-terminal domain, or their functional homolog or derivative; (b) a viral intercellular spreading protein such as herpes simplex virus-1 protein, Marek's disease virus VP22 protein, or their functional homolog or derivative; (c) an endoplasmic reticulum chaperone polypeptide such as calreticulin, ER60, GRP94, gp96, or their functional fragment or derivative; (d) a cytoplasmic translocation polypeptide domains of a pathogen toxin, such as domain II of Pseudomonas exotoxin ETA (ETAdII), or its functional homolog or derivative; (e) a polypeptide that targets the centrosome compartment of a cell, such as gamma-tubulin, or its functional homolog or derivative; or (f) a polypeptide that stimulates dendritic cell processors or activated dendritic cell activity

such as granulocyte monocyte-colony stimulating factor (GM-CSF), Flt3-ligand extracellular domain, or its functional homolog or derivative. The first polypeptide is preferably selected from Mycobacterium tuberculosis HSP70, HSP70 C-terminal domain, HSV-1 VP22, MDV VP22, calreticulin, Pseudomonas ETAdII, GM-CSF, Flt-3 ligand extracellular domain or gamma-tubulin. The first polypeptide can be a transport polypeptide comprising a 301 or 249 residue amino acid sequence, given in the specification. The antigenic polypeptide comprises an epitope that binds to, and is presented in the cell surface by, an MHC class I protein. The epitope is 8-11 amino acid residues in length. The antigen is present on, or cross-reactive with an epitope of, a pathogenic organism (a bacterium), cell or virus, preferably a human papilloma virus. The antigen is the E7 polypeptide of HPV-16 or its antigenic fragment. The pathogenic cell is a tumor cell. The antigen is a tumor-specific or tumor-associated antigen and comprises a peptide of the HER-2/neu protein. The nucleic acid molecule is operatively linked to a promoter. The promoter is expressed in an antigen-presenting cell (APC), preferably a dendritic cell. The alphavirus of the nucleic acid molecule is a Sindbis virus, preferably the replicon SINrep5. The packaging cell line comprises genes encoding capsid and envelope glycoproteins of the alphavirus, which are separated in distinct cassettes to minimize formation of the replication competent virus during replicon production. The packaging cell line is 987dlsplit24. Preferred Cell: The cell preferably expresses the nucleic acid molecule. The cell is an APC, such as dendritic cell, keratinocyte, macrophage, monocyte, B lymphocyte, astrocyte or activated endothelial cell.Preferred Method: Inducing or enhancing an antigen specific immune response in a subject comprises administering the pharmaceutical composition to the subject to induce or enhance immune response. The response is mediated by CD8+ cytotoxic T lymphocytes (CTL) or antibodies. The composition can be administered ex vivo to the cells that comprise APCs. The APCs are dendritic cells and are human APCs . The APCs are isolated from a living subject. The method further comprises administering the ex vivo-treated human cells to a histocompatible human subject. The methods in (5) and (6) comprise administering the pharmaceutical composition to the subject. The nucleic acid molecule, expression vector or cell comprises the antigen. The antigen comprises one or more tumor-associated or tumor-specific epitopes present on the tumor of the subject to inhibit the growth or preventing of the re-growth, or an epitope that binds to, and is presented in the cell surface by, MHC class I proteins to increase the numbers or activity of the CTLs.

ACTIVITY - Cytostatic; Virucide; Protozoacide; Antibacterial; Hepatotropic; Anti-HIV (human immunodeficiency virus). No biological data is given.

MECHANISM OF ACTION - Vaccine.

USE - The nucleic acid molecule, polypeptides and vectors are useful as vaccines for enhancing immune responses, primarily cytotoxic T lymphocytes (CTL) responses to specific antigens (claimed) such as tumor or viral antigens, and for inhibiting growth or preventing re-growth of a tumor. The packaging cell line is useful for generating alphavirus replicon particles without contamination from replicon-competent virus. The pathogenic organisms include viruses such as human papilloma virus, hepatitis B virus, hepatitis C virus, human immunodeficiency virus, Epstein Barr virus and herpes simplex virus, intracellular parasites such as malaria, and bacteria that grow intracellularly such as mycobacteria and listeria.

ADMINISTRATION - Dosage of the nucleic acid or polypeptide is 1 ng-10 mg (preferably 0.01-100 micro-g) per kg. Administration can be intramuscular, intradermal, subcutaneous, intratumoral or peritumoral (all claimed), intravenous, oral, intrathecal, inhalation, transdermal or rectal.

EXAMPLE - For the generation of pcDNA3-VP22/E7, VR22 was subcloned from pcDNA3-E7(E/B), which contains E7 with EcoRI and BamHI restriction

sites on the flanking ends of E7, polymerase chain reaction (PCR) was used to amplify the E7 fragment with pcDNA3-E7 and a set of primers: 5'-gggaattcatggagatacaccta-3'; and 5'- ggtggatccttgagaacgatgg-3'. The amplified product was further cloned into the EcoRI/BamHI sites of pcDNA3. The accuracy or all the DNA constructs was confirmed by sequencing.(93 pages)

L4 ANSWER 16 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2002-12074 BIOTECHDS
TI Novel isolated Her-2/Neu polypeptide composition
useful for therapy, prevention and diagnosis of cancer, preferably breast cancer;
vaccine composition, useful for tumor gene therapy and diagnosis
AU HAND-ZIMMERMANN S; CHEEVER M A; FOY T M; LODES M J; KALOS M D; MCNEILL P D; VEDVICK T S
PA CORIXA CORP
PI WO 2002014503 21 Feb 2002
AI WO 2000-US41733 14 Aug 2000
PRAI US 2001-270520 21 Feb 2001
DT Patent
LA English
OS WPI: 2002-280758 [32]
AN 2002-12074 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - An isolated Her-2/Neu polypeptide composition (I) effective for eliciting an immune response, is new.

DETAILED DESCRIPTION - (I) comprises a sequence of EEYLVPQQGF. INDEPENDENT CLAIMS are also included for the following: (1) an isolated polynucleotide composition (II) effective for eliciting an immune response in a patient, encoding (I); (2) a pharmaceutical composition (III) comprising (I) or (II); and (3) an isolated polynucleotide composition (IV) comprising the T-cell receptor-alpha (TCR-alpha) sequence of 686 amino acids fully defined in the specification or comprising the TCR-beta sequence of 957 amino acids fully defined in the specification.

WIDER DISCLOSURE - The following are disclosed: (i) fragments, variants and/or derivatives of Her-2/Neu polypeptide or polynucleotide sequences; (ii) an expression vector comprising Her-2/Neu polynucleotides; (iii) a host cell transformed or transfected with the above mentioned vector; (iv) a pharmaceutical composition comprising an antibody or its antigen-binding fragment which specifically binds to Her-2/Neu polypeptide, or its fragment, or an antigen presenting cell that expresses a Her-2/Neu polypeptide; (v) a fusion protein comprising Her-2/Neu polypeptide; (vi) a polynucleotide that encodes the above mentioned fusion protein; (vii) a method for removing tumor cells from a biological sample and its use; (viii) isolated T cell population comprising T cells prepared using Her-2/Neu polypeptide or polynucleotide; (ix) determining the presence or absence of cancer in a patient; (x) monitoring the progression of cancer in a patient; (xi) an antibody such as a monoclonal antibody, that binds to Her-2/Neu polypeptide; (xii) a diagnostic kit comprising the above mentioned antibody or one or more oligonucleotide probes or primers; (xiii) TCR specific for Her-2/Neu polypeptide, or for its variant or derivative; (xiv) a mammalian host cell transfected with a polypeptide encoding TCR specific for Her -2/Neu polypeptide; (xv) an assay for detecting mRNA or DNA encoding the above mentioned TCR; (xvi) a formulation comprising T cell and/or antibody compositions; and (xvii) a kit for cancer detection and diagnosis.

BIOTECHNOLOGY - Preparation: (I) is prepared by standard recombinant techniques. Preferred Composition: (III) further comprises an

immunostimulant which comprises an adjuvant.

ACTIVITY - Cytostatic. The ability of Her-2/Neu protein subunit and vaccines to mediate tumor protection was tested. Her-2/Neu vaccines consisting of either full length or truncated forms of Her-2/Neu were evaluated for the ability to elicit a protective immune response against challenge with a syngeneic Her-2/Neu expressing tumor cell line. C57B1/6 mice were immunized with plasmid DNA encoding full length human Her-2/Neu, intracellular binding domain (ICD), or the extracellular binding domain (ECD) portions of Her-2/Neu. Following 2 DNA immunizations, mice were challenged subcutaneously with EL4 cells transfected with full length human Her-2/Neu and tumor growth was monitored. In naive mice, EL-4-Her-2/Neu cells formed large solid tumors within 14-20 days of subcutaneous administration. Vaccination with Her-2/Neu plasmid DNA, either full length, ICD or ECD subunits, substantially inhibited the growth of the tumor cells. To determine whether protein subunit vaccines were also effective at eliciting tumor protection, mice were immunized with ICD or ECD protein plus adjuvant, challenged with EL4-Her-2 /Neu, and monitored for tumor growth. The results demonstrated that vaccination with ICD protein elicited a partially protective immune response in which both the frequency of mice developing tumor and the mean tumor size of mice bearing tumors were decreased.

MECHANISM OF ACTION - Elicitor of immune response ; gene therapy.

USE - (I) or (II) (preferably having a sequence from about nucleotides 2026-3765 of a sequence comprising 3768 base pairs fully defined in the specification) is useful for eliciting an immune response in a patient, where the patient is human leukocyte antigen (HLA)-B44 positive or is affected with breast cancer (claimed). (I) or (II) is useful for the therapy and diagnosis of cancer, preferably breast cancer, in pharmaceutical compositions, e.g., vaccine and other compositions for the diagnosis, prevention and treatment of human malignancies, for stimulating and/or expanding T cells specific for Her-2/Neu polypeptide, and for inhibiting the development of cancer in a patient. (II) is useful for stimulating a T cell response in a human patient, as probe or primer for nucleic acid hybridization, to selectively form duplex molecules with complementary stretches of the entire Her-2/Neu gene or gene fragments of interest, to isolate a full length gene from a suitable library, and to direct expression of a polypeptide in appropriate host cells. (III) is useful in prophylactic or therapeutic applications, and for the treatment of cancer, preferably for the immunotherapy of breast cancer and other Her-2/Neu-associated malignancies.

ADMINISTRATION - (III) is administered by intravenous, intramuscular, intracutaneous, subcutaneous, intranasal or oral route at a dose of 25 mug-5 mg/kg.

EXAMPLE - Identification of an human leukocyte antigen (HLA)-B44-restricted, naturally processed epitope of Her-2/Neu was as follows: The epitope recognized by a T cell clone, 17D5 was characterized. This clone recognized antigen presenting cells (APC) expressing the intracellular binding domain (ICD) or full-length Her-2/Neu protein. The HLA-restriction element for the clone was determined to be HLA-B4402 by using a panel of allogenic cell lines matched at various HLA alleles with the T cell clone as APC in gamma interferon Elispot assays. This was confirmed by transduction of HLA-B44-negative, Her-2/Neu-positive APC with a B4402-recombinant retrovirus to confer recognition. The region of the ICD recognized by the clone was narrowed by using recombinant retrovirus expressing a series of 5 fragments of the ICD to transduce B44+ APC. Recognition (as demonstrated by gamma interferon release) by the clone of 2 of these fragments indicated that the epitope was contained within a

235 amino acid fragment beginning at position 975 in the Her-2/Neu sequence. Predicted B44-binding 9mer and 10mer peptides from within this fragment were chosen and synthesized. Of the 13 peptides synthesized, one was recognized by the clone and determined to be the epitope. This was demonstrated by gamma interferon release and tumor necrosis factor (TNF)-alpha release assays. The sequence of this naturally produced Her-2/Neu epitope was EEYLVPQQGF, at position 1021-1030 in the Her-2/Neu protein sequence. (129 pages)

L4 ANSWER 17 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2002-12065 BIOTECHDS
TI New nucleic acids encoding a fusion polypeptide comprising an endoplasmic reticulum chaperone polypeptide linked to an antigenic polypeptide, useful as a vaccine for inducing antigen-specific immune responses;
plasmid or virus vector-mediated gene transfer and expression in host cell and antibody for use in recombinant vaccine and nucleic acid vaccine preparation and cancer therapy and gene therapy
AU WU T; HUNG C
PA UNIV JOHNS HOPKINS
PI WO 2002012281 14 Feb 2002
AI WO 2000-US24134 3 Aug 2000
PRAI US 2000-222902 3 Aug 2000
DT Patent
LA English
OS WPI: 2002-257463 [30]
AN 2002-12065 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - A nucleic acid molecule (I) encoding a fusion polypeptide comprising a first polypeptide domain comprising an endoplasmic reticulum chaperone polypeptide and a second polypeptide domain comprising at least one antigenic peptide.

DETAILED DESCRIPTION - A nucleic acid molecule (I) encoding a fusion polypeptide useful as a vaccine composition, comprising: (a) a first nucleic acid (S1) encoding a first polypeptide (P1) comprising an endoplasmic reticulum chaperone polypeptide; (b) a linker nucleic acid encoding a linker peptide optionally, fused in frame with S1; and (c) a second nucleic acid (S2) linked in frame to S1 or to the linker nucleic acid sequence, and encodes an antigenic polypeptide or peptide. INDEPENDENT CLAIMS are also included for the following: (1) an expression vector or cassette comprising (I) operatively linked to a promoter, and optionally, additional regulatory sequences that regulate expression of (I) in a eukaryotic cell; (2) a cell, which has been modified to comprise the nucleic acid of expression cassette or vector; (3) a particle comprising (I) or the expression cassette or vector; (4) a fusion of chimeric polypeptide comprising: (a) a first polypeptide comprising an endoplasmic reticulum chaperone polypeptide; and (b) a second polypeptide comprising an antigenic peptide or polypeptide; (5) a pharmaceutical composition capable of inducing or enhancing an antigen-specific immune response, comprising pharmaceutical and immunological excipient in combination with a composition consisting of (I), expression vector or cassette, cell, particle, or the fusion or chimeric polypeptide defined above; (6) methods of inducing or enhancing an antigen specific immune response in a subject; (7) a method of increasing the numbers or lytic activity of CD8+ cytotoxic T lymphocytes (CTLs) specific for a selected antigen in a subject; and (8) a method of inhibiting growth or preventing re-growth of a tumor in a subject.

BIOTECHNOLOGY - Preferred Nucleic Acid: The antigenic peptide comprises an epitope that binds to an MHC class I protein, where the epitope is about 8-11 amino acid residues. The chaperone polypeptide comprises calreticulin (CRT), preferably human calreticulin encoded by the 1889 base pair (bp) nucleotide sequence (II) given in the

specification. The calreticulin polypeptide consists essentially of a sequence of residues 1-180 or 181-417 of the 417 amino acid sequence defined in the specificaton. The chaperone polypeptide is selected from a calnexin polypeptide, an ER60 polypeptide, tapasin polypeptide, GRP94/GP96 polypeptide, a GRP94 polypeptide, and their equivalents. The antigen is present on, or cross-reactive with an epitope of, a pathogenic organism, cell, or virus, where the virus is a human papilloma virus. The antigen is the E7 polypeptide of HPV-16 or its antigenic fragment. The HPV-16 E7 polypeptide is preferably non-oncogenic. The antigen is a tumor-specific, or tumor-associated antigen or its antigenic epitope, preferably the Her-2/neu protein or its peptide. The pathogenic organism is a bacterium, or the pathogenic cell is a tumor cell. (I) is operatively linked to a promoter, which is expressed in an antigen-presenting cell (APC), such as a dendritic cell. Preferred Polypeptide: In the fusion or chimeric polypeptide, the antigenic peptide or polypeptide comprises an epitope that binds to, and is presented on the cell surface by MHC class I proteins. The chaperone polypeptide and the antigenic polypeptide or peptide are linked by a flexible chemical linker. The first polypeptide is N-terminal to the second polypeptide. Alternatively, the second polypeptide is N-terminal to the second polypeptide. The chaperone polypeptide comprises a calreticulin polypeptide or its homologue. The chaperone polypeptide comprises anyone of a tapasin, ER60, an ERP94, or a calnexin polypeptide or its equivalent. Preferred Expression Vector: The expression vector or cassette is a viral vector, a plasmid, or a self-replicating RNA replicon. The self-replicating RNA replicon is a Sindbis virus self-replicating RNA replicon, where the replicon is SINrep5. The chaperone polypeptide comprises a calreticulin polypeptide. The chaperone polypeptide comprises a tapasin, an ER60, an ERP94 of a calnexin polypeptide, or their equivalent. Preferred Cell: The cell expresses the nucleic acid molecule, and is an antigen presenting cell (APC) selected from a dendritic cell, a keratinocyte, a macrophage, a monocyte, a B lymphocyte, a microglial cell, an astrocyte, or an activated endothelial cell. Preferred Particle: The particle comprises a material suitable for introduction into a cell or an animal by particle bombardment. The material is preferably gold. Preferred Method: Inducing or enhancing an antigen specific immune response in a subject comprises administering a pharmaceutical composition defined above. The response is mediated at least in part by CD8+ cytotoxic T lymphocytes (CTL), or by antibodies. The composition is administered to the cells ex vivo, where the cells comprise APCs, specifically dendritic cells of human origin. The method further comprises administering the cells to which the composition was administered ex vivo to a histocompatible subject or to the subject from which the cells were taken. The cells human cells and the subject are human. The composition comprises the nucleic acid molecule, the expression vector or cassette, or the particle, and can also be administered is by biolistic injection. Increasing the numbers or lytic activity of CD8+ CTLs specific for a selected antigen in a subject, or inhibiting growth or preventing re-growth of a tumor in a subject comprises administering a pharmaceutical composition of (5), where the nucleic acid molecule, the expression vector or cassette, the cell, the particle or the fusion or chimeric polypeptide comprises the selected antigen, and the selected antigen comprises an epitope that binds to, and is presented on the cell surface by MHC class I proteins. Inhibiting growth or preventing re-growth of a tumor in a subject comprises administering the pharmaceutical composition of (5), where the nucleic acid molecule, the expression vector or cassette, the cell, the particle or the fusion or chimeric polypeptide comprise one or more tumor-associated or tumor specific epitopes present on the tumor. The method further comprises before, together with or after the administration of the pharmaceutical composition, administering to the subject a second composition having anti-angiogenic activity. The anti-angiogenic composition is angiostatin, endostatin or TIM -2. The method further comprises treating the subject

with radiotherapy or chemotherapy.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Vaccine. Anti-tumor effects mediated by E7-specific immune responses and the vaccine-stimulated anti-angiogenesis effects in vaccinated mice were evaluated. C57BL/6 mice that were vaccinated intradermally with DNA vaccines comprising chimeric calreticulin/E7 (CRT/E7) fusion genes exhibited dramatically increased E7-specific CD8+ T cell precursors, tumor protection, and tumor treatment compared to DNA vaccines containing wild type E7 or CRT genes alone. Treatment of C57BL/6 mice or nude mice with either CRT DNA or chimeric CRT/E7 DNA led to reduction of lung metastatic nodules and inhibition of angiogenesis within the lung nodules. Results indicate that the linkage of CRT gene to an antigen gene may greatly enhance the potency of DNA vaccines to elicit anti-tumor effects through both a significant enhancement of antigen-specific CD8+ T cell immune responses, and anti-angiogenesis effects.

USE - The nucleic acid is useful as a vaccine for inducing enhanced antigen-specific immune responses, particularly those mediated by cytotoxic T lymphocytes. The nucleic acid and compositions comprising the nucleic acid is also useful for inhibiting the growth of a tumor.

ADMINISTRATION - The composition of (5) is administered through intramuscular, intradermal, subcutaneous, intratumoral or peritumoral routes (claimed). The compositions may also be administered systemically, regionally or locally, through intraarterial, intrathecal, intravenous, parenteral, intrapleural cavity, topical, oral, local, subcutaneous, intratracheal, or transmucosal (e.g. buccal, bladder, vaginal, uterine, rectal, nasal mucosa) routes.

EXAMPLE - For the generation of plasmid encoding the full length of rabbit calreticulin (CRT), pcDNA-CRT, the DNA fragment encoding this protein was PCR amplified using rabbit CRT cDNA template and the following primers: 5'-ccggtctagaatgtcgctccctgtgccgct-3'; and 5'-ccggagatctcagctcgtccttggcctggc-3'. The amplified product was digested with XbaI and BamHI, and further cloned into XbaI and BamHI cloning sites of pcDNA3 vector. To generate pcDNA3-CRT/E7, the E7 DNA was PCR amplified suing pcDNA3-E7 as a DNA template, and the primers: 5'-gggaattcatggagatacaccta-3', and 5'-ggtggatccttgagaacagatgg-3'. The amplified E7 DNA fragment was then digested with BamHI and further cloned into the BamHI cloning sites of pcDNA3-DRT vector. The orientation and accuracy of these constructs was confirmed by DNA sequencing. Plasmid DNA with CRT, e7 or CRT/E7 gene insert, and the empty plasmid vector were transfected into subcloning DH5 cells. DNA was then amplified and purified suing double CsCl purification. The integrity of the plasmid DNA and the absence of E. coli DNA or RNA were checked in each preparation using 1% agarose gel electrophoresis. The presence of E7 fragment was confirmed by restriction enzyme digestion and gel electrophoresis.(71 pages)

L4 ANSWER 18 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2002-12060 BIOTECHDS
TI New nucleic acids encoding fusion polypeptide comprising intercellular transport polypeptide linked to antigenic polypeptide, useful as therapeutic vaccine for cancer and major chronic viral infections; vector-mediated recombinant protein gene transfer and expression in host cell, DNA primer and polymerase chain reaction for use in recombinant vaccine preparation and cancer, herpes virus, Marek-disease virus, retro virus andrabies virus infection therapy
AU WU T; HUNG C
PA UNIV JOHNS HOPKINS
PI WO 2002009645 7 Feb 2002
AI WO 2000-US23966 1 Aug 2000
PRAI US 2001-281004 4 Apr 2001
DT Patent
LA English

OS WPI: 2002-257367 [30]
AN 2002-12060 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - A nucleic acid molecule (I) encoding a fusion polypeptide comprising: (a) a first polypeptide (P1) comprising at least one intercellular transport polypeptide; (b) a second polypeptide (P2) comprising at least one antigenic polypeptide or peptide; and (c) optionally, a linker peptide linking the first and second polypeptide, is new.

DETAILED DESCRIPTION - A nucleic acid molecule (I) encoding a fusion polypeptide comprising: (a) a first nucleic acid sequence encodes P1; (b) a linker nucleic acid sequence encoding a linker peptide, optionally, fused in frame with the first nucleic acid sequence; and (c) a second nucleic acid sequence that is linked in frame to the first nucleic acid sequence or to the linker nucleic acid sequence and that encodes an antigenic polypeptide or peptide, is new. INDEPENDENT CLAIMS are also included for the following: (1) an isolated nucleic acid molecule that hybridizes with (I) under stringent hybridization conditions; (2) an expression vector comprising (I) operatively linked to a promoter and optionally, additional regulatory sequences that regulate expression of the nucleic acid in a eukaryotic cell; (3) a cell which has been modified to comprise the (I) or the expression vector; (4) a particle comprising (I) or the expression vector; (5) a fusion polypeptide comprising a first domain consisting of an intercellular transport polypeptide, and a second domain consisting of an antigenic peptide or polypeptide; (6) a pharmaceutical composition capable of inducing or enhancing an antigen-specific immune response, comprising a pharmaceutically and immunologically acceptable excipient in combination with a composition selected from: (a) (I) or expression vector of (2); (b) the cell of (3); (c) the particle of (4); (d) the fusion polypeptide; and (e) any combination of (a)-(d); (7) inducing or enhancing an antigen specific immune response in a subject by administering to the composition of (6); (8) increasing the numbers or lytic activity of CD8+ CTLs specific for a selected antigen in a subject; and (9) inhibiting growth or preventing re-growth of a tumor in a subject.

BIOTECHNOLOGY - Preferred Nucleic Acid: The antigenic polypeptide comprises an epitope that binds to and is presented on the cell surface by a major histocompatibility complex (MHC) class I protein, where the epitope is about 8-11 amino acid residues in length. The transport polypeptide is a viral polypeptide or its homologue, preferably a herpesvirus VP22 polypeptide or its homologue. The intercellular transport polypeptide and the antigenic peptide are linked by a chemical linker, which is a flexible chemical linker. The first domain is N-terminal to the second domain, or the second domain is N-terminal to the first domain. The herpesvirus is a herpes simplex virus or a Marek's disease virus. The antigen is present on or cross-reactive with an epitope of a pathogenic organism, cell, or virus, where the antigen is the E7 polypeptide of human papilloma virus (HPV)-16 or its antigenic fragment, and the virus is a human papilloma virus. The HPV-16 E7 polypeptide is non-oncogenic. The pathogenic organism is a bacterium, and the pathogenic cell is a tumor cell. The antigen is a tumor-specific or tumor-associated antigen, which comprises a peptide of the HER-2/neu protein. (I) is operatively linked to a promoter expressed in an antigen presenting cell (APC), preferably a dendritic cell. Preferred Vector: The expression vector is a viral vector, a plasmid, or is a self-replicating RNA replicon. The self-replicating RNA replicon is a Sindbis virus self-replicating RNA replicon, preferably SINrep5. Preferred Cell: The cell expresses the nucleic acid molecule, and is an APC selected from a dendritic cell, a keratinocyte, a macrophage, a monocyte, a B lymphocyte, a microglial cell, an astrocyte, or an activated endothelial cell. Preferred Particle: The particle comprises a material suitable for introduction into a cell or an animal by particle bombardment. The material is preferably gold. Preferred Method: The

antigen specific immune response is mediated at least in part by CD8+ cytotoxic T lymphocytes (CTL) or by antibodies. The composition is administered ex vivo to the cells, where the cells are APCs specifically dendritic cells. The APCs are human APCs isolated from a living subject. The method further comprises administering the ex vivo-treated cells to a histocompatible subject through intramuscular, intradermal, or subcutaneous route. The composition comprises (I), the expression vector or the particle, and may be administering is by biolistic injection, or by intratumoral or peritumoral means. Increasing the numbers or lytic activity of CD8+ CTLs specific for a selected antigen in a subject, comprises administering a composition comprising (I), the expression vector comprising (I), a cell or particle comprising (I) or the expression vector, a fusion polypeptide defined above, and their combinations. (I), the expression vector, cell, particle or fusion polypeptide comprises the antigen, which consists of an epitope that binds to and is presented on the cell surface by MHC class I proteins. Inhibiting the growth or preventing re-growth of a tumor in a subject, comprises administering to a composition as defined above, where (I), the expression vector, cell, particle or fusion polypeptide comprises the antigen, which consists of one of more tumor-associated or tumor-specific epitopes present on the tumor in the subject. The composition is administered by intratumoral or peritumoral routes. The method further comprises treating the subject with radiotherapy or chemotherapy.

ACTIVITY - Virucide; cytostatic.

MECHANISM OF ACTION - Vaccine. Mice vaccinated with VP22/E7 DNA exhibited greater than 5-fold increase in E7-specific IFN-gamma+ CD8+ T cell precursors (576/3 x 10 to the power of 5 splenocytes) compared to mice vaccinated with wild type E7 DNA 99/3 x 10 to the power of 5 splenocytes). Results indicated that addition of VP22 to E7 significantly enhanced E7-specific CD8+ T cell-mediated immune responses and that fusion of E7 to VP22 was essential for the observed enhancement since VP22 mixed to E7 (VP22+E7 DNA) did not generate enhance of CD8+ cell activity. Linkage of irrelevant proteins (such as GFP) to E7 did not generate enhancement of E7-specific CD8+ cell activity.

USE - The nucleic acid is useful as a vaccine for enhancing immune responses, primarily cytotoxic T lymphocyte responses to specific antigens such as tumor or viral antigens. The compositions comprising the nucleic acids are especially useful as a therapeutic vaccine for cancer and for major chronic viral infections, as well as in the treatment of veterinary herpesvirus infections, including equine or bovine herpesvirus, Marek's disease virus in chickens and other fowls, animal retroviral diseases, pseudorabies, and rabies.

ADMINISTRATION - Administration is by subcutaneous, intradermal, intravenous, intramuscular, oral, intrathecal, inhalation, transdermal, rectal or intratumoral routes. Dosage is 10 mg/kg body weight, preferably 0.1-1 microgram/kg body weight.

EXAMPLE - pcDNA3-VP22 was generated by subcloning VP22 from pVP22/myc-His into the unique EcoRV and BamHI cloning sites of the pcDNA3.1(-) expression vector downstream of the cytomegalovirus (CMV) promoter. pcDNA3-VP22/E7 was generated by subcloning VP22 from pcDNA3-VP22 into the EcoRV-BamHI cloning sites of the pcDNA3-E7. pcDNA3-E7(E/B) was generated by polymerase chain reaction (PCR) amplifying the E7 fragment with pcDNA3-E7 and primers (1) and (2). Amplified product was cloned into the EcoRI/BamHI sites of pcDNA. pCDNA3-VP22(1-267)/E7 was generated by first PCR-amplifying a DNA fragment encoding VP22(1-267) using pcDNA3-VP22 and primers (3) and (4). The amplified product was cloned into the XbaI/EcoRI cloning sites of pcDNA3-E7(E/B). pcDNA3-GFP was generated by PCR-amplifying a DNA fragment encoding GFP with pEGFPN1 DNA and primers (5) and (6). Amplified product was cloned into the BamHI cloning sites of the pcDNA3-GFP. pcDNA3-E7/GFP was constructed by cloning GFP isolated from pcDNA3-GFP into BamHI/HindIII sites of pcD NA3-E7/(E+B). VP/E7/GFP was constructed by amplifying VP22 with primers (7) and (8), and cloning into XbaI/EcoRI

sites of pcDNA3-E7/GFP. pcDNA3-VP22(1-267)/E7/GFP was constructed by cloning VP22(1-267) isolated from pcDNA3-VP22(1-267) into XbaI/EcoRI sites of pcDNA3-E7/GFP. pSC11-VP22/E7 was cloned by isolating VP22 from pcDNA3-VP22/E7 and cloning it into Not/SamI sites of pSC11 vector. pSC11-VP22 was generated by isolating VP22 from pcDNA3-VP22 and cloning it into NotI/SamI sites of pSC11 vector. pcDNA3-TAT/E7 was generated by synthesizing the complementary oligomers (10) and (11) encoding MRKKRRQRRR. The oligomers were annealed and cloned into the XbaI/EcoRI sites of pcDNA3-E7(E/B). For the generation of pcDNA3-E7/MTS, the complementary oligomers (13) and (14) encoding AAVLLPVLLAAP were synthesized. Oligomers were annealed and cloned into the BamHI/HindIII sites of pcDNA3-E7 (E/B). For the generation of pcDNA3-AH/E7, complementary oligomers (16) and (17) encoding MRQIKIWFQNRRMKW KK, were synthesized. Oligomers were annealed and cloned into the XbaI/EcoRI sites of pcDNA3-E7(E/B). (102 pages)

L4 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7
AN 2001:747826 CAPLUS
DN 135:302895
TI Compositions and methods for dendritic cell-based immunotherapy
IN Laus, Reiner; Vidovic, Damir; Graddis, Thomas
PA Dendreon Corporation, USA
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001074855	A2	20011011	WO 2001-US10515	20010330
	WO 2001074855	A3	20020307		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2403964	AA	20011011	CA 2001-2403964	20010330
	AU 2001047919	A5	20011015	AU 2001-47919	20010330
	US 2002061310	A1	20020523	US 2001-821883	20010330
	US 7060279	B2	20060613		
	EP 1272633	A2	20030108	EP 2001-920913	20010330
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003529608	T2	20031007	JP 2001-572544	20010330
	NZ 522066	A	20040827	NZ 2001-522066	20010330
	US 2005232932	A1	20051020	US 2005-144912	20050603
PRAI	US 2000-193504P	P	20000330		
	US 2001-821883	A1	20010330		
	WO 2001-US10515	W	20010330		

AB Disclosed are immunostimulatory fusion proteins and methods for generating protective DC-induced, T cell-mediated immune responses in vitro and in vivo. The immunostimulatory fusion proteins comprise a polypeptide antigen component and an immunostimulatory component derived from the intracellular domain of the HER-2 protein. Also disclosed are immunostimulatory compns. comprising dendritic cells pulsed with such an immunostimulatory fusion protein and methods for immunotherapy using the compns. The fusion protein or fusion protein-pulsed dendritic cells can be used for treatment of cancer.

L4 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:489634 CAPLUS
DN 135:88013
TI Mouse gene Her-2/neu (c-erbB2) polynucleotides and polypeptides, and uses thereof in pharmaceutical compositions and/or vaccines for treatment of breast cancer
IN Spies, A. Gregory
PA Corixa Corp., USA
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001048205	A2	20010705	WO 2000-US35648	20001229
	WO 2001048205	A3	20020207		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-474382 A 19991229
AB The invention provides the mouse Her-2/neu (c-erbB2) oncogene protein, a fusion protein comprising the Her-2/neu protein linked to a T helper epitope not present within the native mouse protein, and polynucleotides encoding said proteins. The invention also provides an expression vector containing a polynucleotide encoding the mouse Her-2/neu protein, and a host cell transformed with said vector. The invention further provides a pharmaceutical composition comprised of said polynucleotides, polypeptides, or antigen presenting cells (such as dendritic cells or macrophages) expressing the mouse Her-2/neu protein, and the use of said pharmaceutical composition in inhibiting the development of cancer (such as breast cancer) in a patient. Still further, the invention provides: (1) a vaccine comprised of said polynucleotides, polypeptides, or antigen-presenting cells expressing the Her-2/neu protein, and a non-specific immune response enhancer (adjuvant) that induces a predominantly type I response, and (2) for the use of said vaccine in inhibiting the development of cancer in a patient. Finally, the invention provides: (1) a method for removing tumor cells from a biol. sample which involves contacting sample with T cells that specifically react with the mouse Her-2/neu proteins, (2) a method for stimulating and/or expanding T cells specific for the Her-2/neu protein, which involves the use of said polynucleotides, polypeptides or antigen-presenting cells, and (3) use of isolated said T cell in treatment of cancer. The cDNA sequence, as well as the corresponding amino acid sequence of mouse Her-2 /neu protein are disclosed.

L4 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:100935 CAPLUS
DN 134:161876
TI Fusion proteins of B- and T-cell epitopes of the HER-2 protein for use in cancer vaccines
IN Kaumaya, Pravin T.; Stevens, Vernon C.; Triozzi, Pierre L.
PA The Ohio State University, USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001008636	A2	20010208	WO 2000-US21222	20000803
	WO 2001008636	C1	20020808		
	W: AU, CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 2000066203	A5	20010219	AU 2000-66203	20000803
	EP 1246597	A2	20021009	EP 2000-953823	20000803
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	JP 2003530074	T2	20031014	JP 2001-513369	20000803
	US 7060284	B1	20060613	US 2000-632036	20000803
PRAI	US 1999-146869P	P	19990803		
	WO 2000-US21222	W	20000803		

AB Compns. for stimulating the immune system and for treating malignancies associated with overexpression of the HER-2 protein are provided. Such compns. include immunogenic epitopes of the HER-2 proteins and chimeric and multivalent peptides which comprise such epitopes. The present invention also relates to polynucleotides which encode the chimeric peptides. Also provided are pharmaceutical compns. comprising such immunogenic compns. Methods for stimulating an immune response to HER-2 protein are provided. Methods for treating breast cancer, ovarian cancer, prostate cancer, colon cancer and lung cancer are provided. Mice immunized with these peptides mounted a very strong immune response with antibody titers for some peptides reaching >250,000 with IgG1 and IgG2 as the major isotype.

L4 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8
AN 2000:535278 CAPLUS
DN 133:148720
TI Antigenic deletion derivatives of the Her-2/neu protein for use in vaccines agains breast cancer
IN Cheever, Martin A.; Gheysen, Dirk
PA Corixa Corporation, USA; Smithkline Beecham
SO PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000044899	A1	20000803	WO 2000-US2164	20000128
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2361009	AA	20000803	CA 2000-2361009	20000128
	AU 2000027426	A5	20000818	AU 2000-27426	20000128
	AU 780109	B2	20050303		
	EP 1147190	A1	20011024	EP 2000-905800	20000128
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	TR 200102191	T2	20011221	TR 2001-2191	20000128
	BR 2000007840	A	20020122	BR 2000-7840	20000128
	JP 2002535004	T2	20021022	JP 2000-596141	20000128

	NZ 513062	A	20031031	NZ 2000-513062	20000128
	US 2002177567	A1	20021128	US 2001-854356	20010509
	ZA 2001006179	A	20021028	ZA 2001-6179	20010726
	NO 2001003701	A	20010928	NO 2001-3701	20010727
	HK 1044798	A1	20051230	HK 2002-106267	20020826
	AU 2005202415	A1	20050630	AU 2005-202415	20050603
PRAI	US 1999-117976P	P	19990129		
	AU 2000-27426	A3	20000128		
	US 2000-493480	A3	20000128		
	WO 2000-US2164	W	20000128		

AB Derivs. of the HER-2/neu protein that can be manufactured in useful yields and that retain antigenicity are described for use in pharmaceutical compns. (e.g. vaccines). Specific fusion products of the intracellular and extracellular domains and the genes encoding them are described. The present invention is also directed to methods of treating or preventing cancer by eliciting or enhancing an immune response to the HER-2/neu protein, including for uses in the treatment of malignancies associated with the HER-2/neu oncogene. A series of C-terminal deletion derivs. of rat and human protein covering the amino acids 532-651 were prepared and tested for their yields in animal cell systems. It was found that the kinase domain inhibited export of the protein from the cell but that the phosphorylation domain did not. Fusion proteins of the extracellular domain and the phosphorylation domain were manufactured in Escherichia coli, Pichia pastoris, and CHO cells. The individual domains may be prepared sep. and joined by a non-peptide linker.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 25 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V. on STN

AN 1999010311 ESBIOBASE

TI Redirecting effector T cells through their IL-2 receptors

AU Lustgarten J.; Marks J.; Sherman L.A.

CS Dr. L.A. Sherman, Scripps Research Institute, IMM-15, 10550 North Torrey Pines Road, San Diego, CA 92037, United States.
E-mail: Isherman@scripps.edu

SO Journal of Immunology, (01 JAN 1999), 162/1 (359-365), 32 reference(s)
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DT Journal; Article

CY United States

LA English

SL English

AB Fusion proteins constructed of a tumor-specific Ab joined to IL-2 (Ab- IL-2) have been used in the past to deliver cytokine directly to the site of tumor cells in vivo. These molecules mimic the activity of IL-2 and assist in activating and expanding antitumor effector cells. To enhance the cytolytic activity of CTL specific for peptide epitopes of the Her-2/neu tumor Ag presented by HLA-A*0201 molecules, a fusion protein was constructed consisting of a single chain Ab specific for Her-2/neu, linked to IL-2 (neu- Ab-IL-2). When added to a mixture of tumor cells and Her-2/neu-specific CTL, the protein was found to augment lysis of tumor cells. In addition, the hybrid molecule also promoted lysis of Her-2/neu expressing tumors by non- tumor-specific cloned T cell lines, including Th1 CD4 cells. Analysis of the mechanism of cytotoxicity revealed that the fusion protein mediates the formation of stable conjugates between T cells expressing IL-2R and tumor cells expressing Her-2/neu, resulting in lysis through the Fas-Fas ligand pathway. Lysis induction was independent of specific engagement by the TCR. When tested for its ability to enhance tumor cell eradication by Her-2/neu- specific CD8.sup.+ T cells in an adoptive transfer model in SCID mice, neu-Ab- IL-2 facilitated the elimination of

tumor cells in vivo. Surprisingly, the combination of non-tumor-specific CD8.sup.+ T cells and fusion protein also induced a significant delay of tumor growth. This represents a novel approach for redirecting non-tumor-specific T cells to eliminate tumors.

L4 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 9
AN 1999:586525 CAPLUS
DN 132:106679
TI Preparation and characterization of a recombinant humanized single-chain Fv antibody/human interleukin-2 fusion protein directed against the HER-2/neu (c-erbB2) proto-oncogene product, p185
AU Li, J.; Gyorffy, S. F.; Ring, D. B.; Kwok, C. S.; Austin, R. C.
CS Hamilton Civic Hospitals Research Centre and Department of Pathology, McMaster University, ON, Can.
SO Tumor Targeting (1999), 4(2), 105-114
CODEN: TUTAF9; ISSN: 1351-8488
PB Stockton Press
DT Journal
LA English
AB High dose recombinant human interleukin 2 (rhIL-2) therapy has been used in the treatment of established tumors in both animal models and patients with advanced melanoma or renal carcinoma. However, because high dose rhIL-2 therapy causes severe systemic toxicity in normal tissues, its clin. use has been limited. Therefore, targeting interleukin-2 (IL-2) to the tumor site should improve its anti-tumor-immune response and decrease its systemic toxicity. In this study, we describe the preparation and characterization of a recombinant humanized single-chain Fv(sFv) antibody/IL-2 fusion protein. This recombinant fusion protein consists of humanized variable heavy (VH) and light (VL) domains of monoclonal antibody (mAb) 520C9 directed against the human HER-2/neu(c-erbB2) proto-oncogene product p185 and human IL-2. The fusion protein was stably expressed in baby hamster kidney cells and shown to retain the immunostimulatory activities of IL-2 as measured by IL-2-dependent cell proliferation and cytotoxicity assays. In addition to its IL-2 activity, this fusion protein also possesses binding specificity against the HER-2/neu(c-erbB2) proto-oncogene product, p185, as determined by enzyme linked immunosorbent assay using SKOV 3i.p.1 cells. Taken together, these findings suggest that this recombinant humanized sFv antibody/IL-2 fusion protein may provide an effective means of targeting therapeutic doses of IL-2 to p185 pos. tumors without increasing systemic toxicity or immunogenicity.
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1995:283272 CAPLUS
DN 122:46470
TI Targetted inhibition of tumor growth with viral vectors expressing genes for tumor inhibitors
IN Barber, Jack R.; Jolly, Douglas J.; Respess, James G.
PA Viagene, Inc., USA
SO PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 16

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9421792	A2	19940929	WO 1994-US2951	19940317
	WO 9421792	A3	19950105		

W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KG, KP, KR, KZ,

LK, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US	5662896	A	19970902	US 1993-32846	19930317
AU	9464119	A1	19941011	AU 1994-64119	19940317
EP	689593	A1	19960103	EP 1994-911647	19940317
EP	689593	B1	20060531		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

JP	09503740	T2	19970415	JP 1994-521263	19940317
PRAI US	1993-32846	A	19930317		
US	1988-170515	B2	19880321		
US	1989-395932	B2	19890818		
US	1990-565606	B2	19900810		
US	1990-586603	B1	19900921		
US	1992-965084	B2	19921022		
WO	1994-US2951	W	19940317		

AB A method for inhibiting tumor growth by targetting inhibitory genes or gene products to tumor cells using using cell type-specific viruses carrying the genes is described. Anti-tumor agents include immune activators and tumor proliferation inhibitors. A retroviral expression vector based on Moloney murine leukemia virus was constructed and the gene for mouse or human interferon γ introduced into the proviral DNA under control of the 5'-LTR. Murine tumor cell lines infected with the virus showed an increase in the levels of MHC Class I antigens than did control cells. In comparison, cells treated with interferon γ showed a decrease in levels of Class I MHC. Cells expressing the interferon γ gene elicited a stronger immune response when injected into C57BL/6 mice than did control cells.